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THE PROBLEM OF TYPHOID FEVER IN BALTIMORE.

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AND

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During the past year the city of Baltimore has suffered from a serious and costly epidemic of typhoid fever. From January 1, 1910, to January 1, 1911, 235 deaths from this disease were reported to the Board of Health, while for the same time the total number of cases equaled 1890. The majority of these cases developed during the summer and autumn months, as is shown on Charts I and II. Up to July 1 but 44 deaths and 193 cases had been found, but beginning with this month the disease began to show a greater prevalence. During July, 7 deaths and 110 cases were reported; during August, 30 deaths and 473 cases; during September, 49 deaths and 398 cases; during October, 42 deaths and 359 cases. The two subsequent months, November and December, showed some falling off in both case incidence and fatality, 37 deaths and 251 cases occurring in November and 26 deaths and 106 cases in December. As the cold weather of 1911 became more settled the cases diminished in number, 55 cases and 11 deaths appearing in January, 31 cases and 3 deaths in February, and but 35 cases and 5 deaths in March.

Chart I.—Typhoid Fever in Baltimore, January, 1910, to June, 1911.

	Case Incidence.	Deaths.		Case Incidence.	Deaths.
1910.	Jan. ... 39	7	1910.	Oct 359	42
	Feb. 25	11		Nov. ...251	37
	Mar. ... 30	12		Dec. ...106	26
	April .. 22	4	1911.	Jan. ... 55	11
	May ... 31	2		Feb. ... 31	3
	June ... 46	8		Mar. ... 35	5
	July ...110	7		April... 44	8
	Aug. ...473	30		May ... 56	7
	Sept. ..398	49			

During the year 1909 there were 136 deaths from typhoid and 1069 cases; during 1908, 180 deaths and 1426 cases; in 1907, 230 deaths and 1417 cases. Thus the year 1910 shows more typhoid fever than does any previous year for a considerable period of time. The number of cases recorded in the Department of Health is the largest since vital statistics have been kept in Baltimore, and the number of deaths is only equalled by the figure for the year 1890, when 247 fatalities from this disease were reported.

The deaths in the summer and autumn months also show a great increase over the corresponding months of last year. In 1909, 20 deaths occurred during August, but in 1910 this

rose to 30. For September the number rose from 24 to 49; for October from 23 to 42; for November from 10 to 37; while in December the deaths rose from 9 to 26, as is shown in Chart III.

CHART II.—Typhoid fever in Baltimore. January, 1910, to June, 1911. Case incidence.

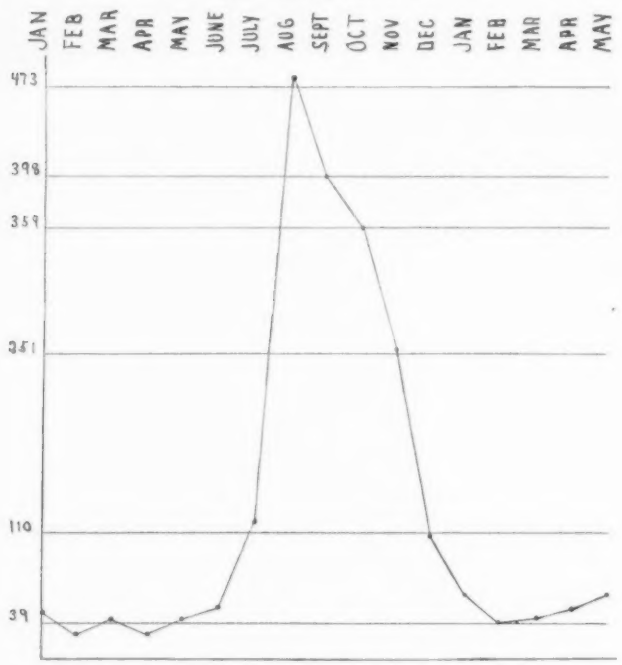
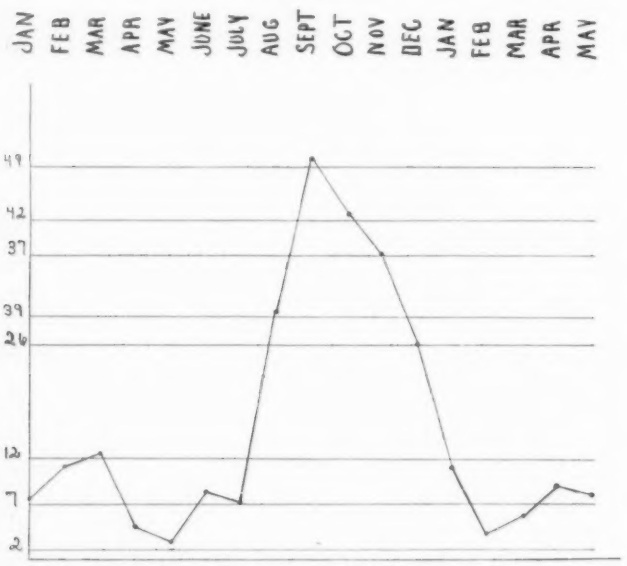


CHART III.—Typhoid fever in Baltimore. January, 1910, to June, 1911. Mortality.



While these figures indicate an increase in typhoid fever during the year just past, compared with preceding years, it must not be supposed that this predominance of the disease in any one particular period has not previously been noted. Thus, in the year 1907 there were 230, and in the year 1902 220 deaths. As can be seen from Chart IV, typhoid fever has always existed in the city of Baltimore. Deaths from it were first reported officially to the Board of Health about the year 1875. At the end of this year 187 deaths were assigned to this cause. Since then statistics of the Department indicate a constant recurrence of the disease from year to year. During the earlier years the diagnosis did not rest upon such secure grounds as at present, the possibility existing that cases of malaria and early tuberculosis might be included among the cases diagnosed as typhoid. Gradually, however, as the symptomatology of the disease became better understood, as the diagnosis of malaria and tuberculosis was more frequently made on the evidence of the parasites and not merely upon the symptoms, and finally as the Widal reaction was introduced, rendering

CHART IV.—Typhoid fever in Baltimore.

Average deaths 1875 to 1880 ..... 183 per year.
Average deaths 1880 to 1885 ..... 167 per year.
Average deaths 1885 to 1890 ..... 162 per year.
Average deaths 1890 to 1895 ..... 207 per year.

Year.	Cases Reported.	Deaths.	Per cent.	Population.
1895	260	173	66.53	479,907
1896	472	188	39.83	493,147
1897	363	189	52.06	506,398
1898	545	189	34.68	541,000
1899	462	153	33.11	541,000
1900	871	189	21.70	541,000
1901	792	141	17.80	518,000
1902	1086	220	20.26	535,000
1903	768	189	24.61	533,000
1904	916	199	21.72	541,000
1905	1019	197	19.33	550,000
1906	1215	183	15.06	558,000
1907	1417	230	16.23	565,000
1908	1426	180	12.62	573,000
1909	1069	136	12.72	581,000
1910	1890	235	12.43	585,000

the recognition of typhoid infection much more certain, the returns made to the Board of Health have become more and more accurate. Despite the fact that some of the cases formerly considered typhoid fever would now be separated from this group, the figures indicate that there has been a gradual diminution in the amount of this disease in the city of Baltimore, as compared with our increasing population. In 1890 we had possibly the largest number of deaths from typhoid ever known here, 247 in an estimated population of 413,000. But since then the number of deaths has diminished annually, the smallest number being reported in 1909, 136 in an estimated population of 580,000.

Beginning with the year 1895 typhoid fever became a notifiable disease in Baltimore, and since then our information has become still more exact. In that year 173 deaths were reported, and 260 cases, a mortality percentage of over 66. The notifications sent to the Board of Health have increased annually, the ratio of death to case incidence constantly falling until in the year 1908 it became 12.62%. That is, during that year

180 deaths from typhoid occurred and 1426 cases were reported. Since the death rate from typhoid fever in hospitals varies from 7 to 20% and in private practice from 5 to 12%, and the usual figure for estimating the number of cases of typhoid, based upon the number of deaths, is 10%, it is evident that we have in Baltimore at the present time very complete returns for this disease.

The officials of the Board of Health, particularly Dr. Jones and Dr. Stokes, have been interested in this complicated and serious problem of typhoid fever for some time, and in the annual report issued by Dr. Bosley for the Health Department for 1907, Dr. Jones has considered the matter at great length and any observations that can be made upon the disease here must start with his paper as the basis.[1]

In discussing this question, Dr. Jones came to the conclusion that 10 possible sources of our typhoid might be named:

1. Bathing in polluted water.
2. Privy wells.
3. Flies.
4. Importation.
5. Contact.
6. Hydrants in yards.
7. Water wells.
8. Raw foods.
9. Milk.
10. Drinking water.

When we now come to a consideration of these possible sources we are confronted with apparently a hopeless task. The factors which enter into the situation are so diversified, our information concerning the disease in general is so defective in those very points which are of prime importance in elucidating the problem, especially the conditions which govern the life history of the responsible parasite outside the human body, that with the evidence at hand it almost seems as though any deductions which we can make must be based upon insufficient grounds. Investigations of typhoid fever in other cities where the conditions are not unlike those in Baltimore, especially in Washington and in Richmond, while fruitful scientifically and slowly solving the problem for those communities, nevertheless do not give us conclusions which can be applied without great caution to our own city. The problem is essentially one which must be worked out by each center of population for itself.

Our typhoid fever may be said to present three definite aspects. First, it has existed in Baltimore from the earliest times, fluctuating somewhat from year to year, never falling below a certain level, but occasionally rising above this level to a point, as in the year 1910, where it may be regarded as epidemic. Secondly, the disease arises essentially as a result of local conditions. There is little or no evidence that our typhoid fever is imported from other districts. We have in our midst the very influences which lead to its continuous propagation. Thirdly, with the exception of the year 1906, when several small epidemics occurred during the colder months and were clearly due to polluted milk supplies, the cases occurring exclusively among the patrons of certain dairies, we have little winter typhoid compared with our *marked summer rise*. Chart I for the year 1910, prepared from the Board of Health Reports, shows this very clearly. But it must be remembered that the variation here represented is not characteristic of any particular year, but represents a distribution of the disease by months which is peculiar for our typhoid. While we usually have but few cases of the disease in the winter months, it never disappears entirely. *Typhoid fever with us is a winter as well as a summer disease.* With the onset of warm weather, however, the case incidence and the number of deaths show a very rapid increase. During July the figures for both run up rapidly; during August they increase still more and the maximum is reached usually in September or in October. With the beginning of cold weather in the autumn the number of cases begins to diminish; this diminution becomes marked in November and December, but at no time do the cases entirely disappear. During the months of January, February, and March the disease remains quiescent only to break out again during the next warm season with the most dreadful certainty. A repetition of the summer epidemic each year can be predicted with absolute confidence.

We have thus two constants, the *continued presence* of the disease in Baltimore, and the *marked seasonal variation.* Dr. Jones, in considering the ten possible sources of typhoid fever which we have previously mentioned, has been able to eliminate such factors as bathing in polluted waters, well water, hydrants in yards, privy vaults and importation, from responsibility as epidemiological factors. Five possible sources of typhoid remain for us to consider.

1. *Raw foods.*—A number of articles of diet which are eaten raw, such as shellfish, vegetables and fruits, are popularly supposed to be intimately associated with enteric fever, and there can be no doubt that the typhoid bacillus may be carried by uncooked foods in certain special instances. Typhoid due to oysters polluted with sewage has been reported by Conn[2] and recently Buchan[3] has called attention to the serious contamination of the shellfish sold in Birmingham, England, and has indicated their importance as a possible source of the disease. As far as oysters are concerned in Baltimore, they may probably be eliminated from responsibility. Our typhoid is at its lowest ebb at the very time when oysters are consumed in the greatest quantity and has its especial prevalence in the months when the sale of the bivalve is forbidden by law. While raw fruits and uncooked vegetables may play a part in the spread of the disease, no satisfactory proof of this has thus far been presented.

2. *Contact.*—Our knowledge of the "chronic bacillus carrier" and the disastrous results which follow his entrance into a family or into a community has served to again emphasize the importance of contact infection in enteric fever. The many investigations in Germany, England, and in this country, especially in New York and Washington, indicate how many of our typhoid patients have previously come into close association with cases of the same disease, especially in its milder forms. They also serve to show that many attacks

which on first consideration cannot be explained on the basis of contact, on careful study and search are apparently clearly the result of a more or less intimate connection with previous cases. In this city we may probably have underestimated the proportion of cases of this character, and Baetjer [4] has recently called attention to the important rôle which contact may play in our country typhoid, reporting 17 cases in two houses. During the past summer direct infection may have had a very significant part in spreading the disease, especially in the poorer sections of the city. The newspapers frequently stated that several cases had been found in one house or in one family. In a certain instance an extraordinarily large number was reported from a block of houses on East Chase street, and here the infectious material seems to have been transmitted directly from person to person. In general, however, the records of the Health Department indicate that in the majority of instances the cases of the disease occur singly in houses, but a small number of two-case and three-case houses having been discovered. Furthermore, we have typhoid summer and winter alike and the factor of contact infection will not explain the great increase of the disease in the summer months—that is, the marked *seasonal variation* or *summer rise*.

3. *Flies.*—One of the most attractive and plausible theories to explain a great prevalence of enteric fever in any community during the hot days of summer is to attribute the spread of infection from individual to individual to the agency of flies. The work of Levy and Freeman [5] in Richmond, where a campaign directed against the fly seemed to be effective in limiting the cases of typhoid in that city, has been quoted far and wide and the conclusions reached by these authors frequently applied to such cities as Washington and Baltimore, where the climatic conditions and character of the population are almost identical with those of Richmond. The importance of the house-fly as the carrier of infection has also been emphasized by Jackson [6] in New York, in seeking an explanation for the cases which appear in that metropolis. Still it must be remembered that in this city we suffer from typhoid not only during the fly season but during many months of the year when responsibility cannot be fastened upon these pests. During the year 1910 we had 26 deaths from typhoid fever and 106 new cases reported to the Board of Health for the month of December. While flies may be carriers of infection during the season when they are especially abundant and may thus explain the increase of the disease during July, August and September, they can play but a subsidiary rôle in the cases which occur during the winter, the early spring, and the late fall. Furthermore a great deal more knowledge as to the life-habits of these insects and the occurrence and distribution of the various species in Baltimore must be obtained before we can justly conclude that their activities are important epidemiological factors in this community.

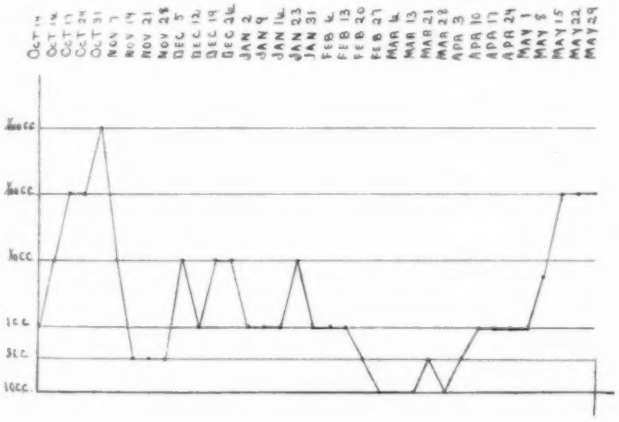
4. *Milk.*—The milk supply of Baltimore comes from a wide district of farming land in the more or less immediate vicinity of the city. It is handled by a number of dairy companies which either produce it on their own premises or collect it from small farmers, and then ship it in bottles or in large cans holding a number of gallons, to the principal railroad stations. During transit no attempts at refrigeration are made. From the stations in the city it is distributed in wagons from house to house or sold directly to the consumer in the little shops dispersed through the poorer sections of the community. Considerable time necessarily elapses between the hour of milking and the ultimate consumption of the product. The various dairies often handle milk from a number of different sources, this milk being mixed in bulk and again parceled out in small quantities. As a result the individual samples sold over the counter may sometimes represent milk collected from widely scattered areas. The inspection of milk in the city limits is wisely carried out by the officials of the Health Department and is as effective as the present laws permit. Still a proper and thorough regulation of the traffic at the proper point, that is, on the premises of the farmers who make a business of producing the milk, is not possible. The larger and more prosperous milk dealers have adopted the modern sanitary regulations which ensure cleanliness and are making conscientious efforts to furnish our citizens with a product which will meet the present-day demand for milk of a proper chemical composition and a low bacterial count. In many of the small shops, however, where milk is sold by the quart, pint, or even half-pint, the filthiest conditions prevail. Refrigeration is either not regarded as necessary or the measures which are carried out are of little value in maintaining the milk at a low temperature. The milk cans are frequently opened as the milk is doled out to the consumers one after another, and since the rooms where the milk is sold are often the living rooms of a large family, it is thus exposed to contamination of various descriptions.

For a number of years now we have been making frequent examinations of the milk found in the poorer quarters of the city in the vicinity of the Johns Hopkins Hospital. While these examinations have not been made through the entire year, nor with sufficient frequency to furnish positive conclusions, they indicate clearly that much of the milk sold to the poor people is badly polluted. The bacterial count frequently runs up into the millions and is uniformly above even the most liberal standards of purity. Recently one of our advanced students, Mrs. de Angulo, has been making weekly examinations of samples of milk collected in East Baltimore. In some instances she has found 50,000,000 bacteria to the cubic centimeter. In a number of cases the count varied from 10,000,000 to 25,000,000, and in nearly every sample obtained at the small shops where the milk is sold from milk cans the count has been 3,000,000 or over. If such a degree of pollution is found during the winter months, what must be the amount of bacterial life in this product in the hot summer weather? Such extremely dangerous conditions are found, of course, only in certain regions and in the small shops. The bottled milk furnished by the better dairies shows usually a low bacterial count, and indeed certain companies furnish milk which would

pass the most rigid qualifications that could be reasonably imposed.

5. *Water.*—The far-reaching importance which must be attached to the Baltimore City Water Supply as a source of our typhoid fever has previously been indicated. Our water is derived from two main streams, the Gunpowder River and Jones Falls. For many years we have made a study of the Gunpowder water and have demonstrated with great regularity a serious and constant pollution in it.[1] *Bacillus coli* can always be obtained in the majority of 1 cc. samples examined. It is frequently present in a dilution of 1/10 and rarely in higher dilutions, 1/100. Together with this organism there are many other bacteria of intestinal origin. *Bacillus alkaligenes,* which so closely resembles the typhoid bacillus, is often found on the plates and certain liquefying bacteria such as *Bacillus cloacae,* which may be regarded as characteristic of sewage, are occasionally encountered. The bacterial count varies greatly, apparently bearing some ratio to the rainfall and amount of water in the reservoirs. It is usually somewhat under a thousand to the cubic centimeter, but may exceed this number,

CHART V.—Pollution of Gunpowder water. Fermenting organisms. October, 1910, to June, 1911.

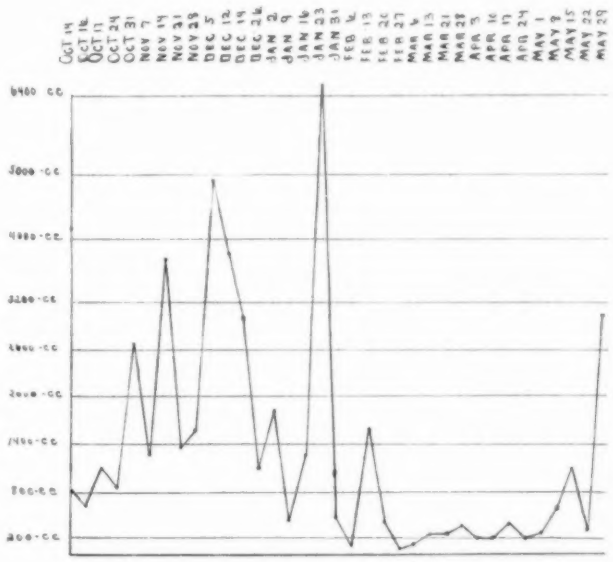


running up to between ten and fifteen thousand. The examination of the water taken from the spigot thus shows a pollution which is of a decidedly serious character and practically permanent. The findings at the tap are amply explained by the conditions which prevail along the watershed of the Gunpowder River. The sewage from numerous farm houses and small settlements of working people passes directly into this stream or into its tributaries, certain of which, notably Western Run, Beaver Dam Run and the Oregon Branch, are grossly polluted.

Dr. Stokes at the Board of Health has obtained much the same results as ours in regard to the Gunpowder water. In addition he has made a special study of Jones Falls and Lake Roland, and he and Hachtel have even succeeded in isolating the typhoid bacillus from Towson Run, one of the small streams which passes into the latter body of water.[2]

Beginning in October, 1910, when typhoid fever was raging in the city of Baltimore, we have made regular tests of the Gunpowder water, estimating the extent of pollution by using the fermentation tube and by counting the number of colonies. The bacteria present at various periods have been isolated and submitted to careful study and identification, largely in the hope that we might determine the value which should be assigned to the presence of various liquefiers. As can be seen from Charts V and VI, the pollution of the water in October had reached a most dangerous grade. *Bacillus coli* or some other fermenting species was constantly present in a dilution of 1/100 and on one occasion in a dilution of 1/1000. The number of microorganisms was also much above that usually accepted as the standard of purity. At this time Maryland had been suffering from a prolonged drought, and the water in

CHART VI.—Pollution of Gunpowder water. Bacterial count. October, 1910, to June, 1911.



Loch Raven and in the Gunpowder was at the lowest ebb it had reached for years. The filth which is regularly present in the stream had evidently been greatly concentrated and the appearance of several thousand colonies to the cubic centimeter and especially the extraordinary degree to which the water could be diluted without causing the disappearance of the intestinal bacteria indicate how totally unfit for use the Gunpowder water was at this time. The pollution of this stream, which was then the main supply of the city, Lake Roland having been temporarily eliminated, continued excessive during the autumn months and early winter. Not indeed till February of this year did conditions improve, the bacterial count come down to normal and the intestinal microorganisms disappear from the fermentation tubes. Recently, however, evidences of sewage contamination are again shown by our studies and during the month of May, 1911, the Gunpowder water reassumed the filthy character it presented last October.

Discussion.

It may thus be seen that with the evidence at hand but an unimportant rôle can be assigned to raw foods, to contact infection, and to flies as epidemiological factors in our typhoid fever. While a certain proportion of our cases may be due to contact and while the number of cases may be augmented through the agency of flies in the fly season, the activity of these insects cannot be made to explain our winter typhoid, nor can the agency of contact explain our great summer rise. A combination of the two factors might be suggested to explain summer and winter typhoid alike, but the problem is not so simple and two other possible sources of infection must be considered. These other possible sources are *milk* and *water*. The milk supplied to the people of Baltimore, especially to the poorer classes, is frequently loaded with microorganisms and would not meet any reasonable requirements based upon a bacteriological examination. The regulations adopted by other cities if applied to Baltimore would probably stop the sale of much of the milk now offered in certain of the crowded districts of the city. This milk pollution is amply explained by the conditions on dairy farms, along the route of travel, and in the shops where the milk is sold. In the long and tortuous journey which the milk drunk in Baltimore must travel from the udder of the cow to the mouth of the consumer, this valuable and almost indispensable article of diet is exposed to frequent chances of contamination with dust, dirt and filth. The abortive attempts at refrigeration are manifestly insufficient to prevent the growth and multiplication of those microorganisms which find accidental entrance. If milk can serve as a source of typhoid fever, we have in the city of Baltimore at the present time ideal conditions for the spread of this disease. Furthermore, the very months of the year when the cases are at their maximum are those months when we can reasonably suppose that the life of the typhoid bacillus in milk will be considerably prolonged, namely, in the hot summer season. Moreover, several outbreaks of the disease in the winter months have been definitely traced to certain dairies, as in the year 1906. Whether the uniform distribution of the cases of typhoid over the entire city which is characteristic of Baltimore can be brought into harmony with milk-borne infection is not quite clear. It must be said, however, that the typhoid of Washington seems to bear a direct relation to the city milk supply, and yet the distribution of the disease in that city is fairly uniform and is similar to the distribution which has been noted here. Thus the utmost stress must be laid upon milk in considering the epidemiology of our typhoid and next to our water supply milk must be regarded as the factor of the greatest importance.

The serious and dangerous pollution of our city water, which has been emphasized by Dr. Stokes and by ourselves, may well be pointed to whenever the subject of typhoid fever is under discussion. That the contamination has been increasing markedly during the past two or three years is evident from the results of the many examinations which have been made. Recent experience in both Richmond and Washington, however, indicates how dangerous it may be to attribute enteric fever to water supplies, even though the filtration of water in other cities or the change from a polluted to a pure supply has been followed by a marked reduction of the typhoid. Still one point of great importance has been brought out by the investigations of the past year. The extent of pollution of the Gunpowder water, or the concentration of the sewage present in it, shows the same variation as does our typhoid fever. Thus typhoid was as its height in September, October and November of last year, and at this time the water used in Baltimore was showing its maximum pollution. By December the number of cases had come down markedly but not to anything like our normal for this month. At the same time, the pollution of the water had diminished in quantity. During the past winter months the typhoid almost disappeared from our midst, and for this period the water showed comparatively little sewage. With the onset of hot weather the pollution of the water supply has again become excessive and the returns to the Department of Health indicate that our typhoid is also becoming prevalent.

Whether this close correspondence or parallelism between the amount of this disease in our city and the extent to which our water supply is polluted is anything more than a coincidence cannot be decided with the evidence at hand. Mere parallelism is no proof of etiological relationship, and until we are able to eliminate water as a factor in the existence of typhoid in Baltimore by the adoption of filtration plants or by its sterilization or disinfection we will not be in a position to explain the disease satisfactorily. For the present the question has only a theoretical interest. Our constantly and persistently polluted water must be regarded for the present as the main source of our typhoid fever. It is absolutely essential for the health of the citizens of Baltimore that the most stringent regulations be enforced in controlling our water supply, and that every effort be made to hasten the construction of the sand filters now being prepared for the Gunpowder water. Until these filters can be utilized the water should be sterilized by the addition of some chemical disinfectant, preferably by the hypochlorite or bleaching powder method.

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THE RECENT EPIDEMIC OF DIPHTHERIA IN THE JOHNS HOPKINS HOSPITAL AND MEDICAL SCHOOL: GENERAL PROCEDURES ADOPTED.*

By WILLIAM W. FORD, M. D., D. P. H.,

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During the last week in January and the first two weeks of February of this year (1911) a number of cases of diphtheria occurred in the Johns Hopkins Hospital and Medical School. On January 25, a pupil nurse with the disease was admitted to the Isolation Ward, and on February 3 a patient in the men's ward, Ward F, developed clinical symptoms of diphtheria, and a throat culture showed the Klebs-Loeffler bacillus. He was immediately isolated and no further cases appeared at that time in the ward from which he was taken. On February 9, a pupil nurse in charge of the children in Ward G, the women and children's ward, developed diphtheria and on the following day an employee in the baggage room was found with an infected throat. These cases all presented the clinical picture of a mild type of the disease and rapidly recovered. On February 11, a child in Ward G, an old burn and skin-grafting case, exhibited a bloody nasal discharge. It had been fretful and ailing for some time and the attention of both doctors and nurses had been directed to its condition. When the discharge appeared it was at once examined and the diagnosis of nasal diphtheria established. This infection proved to be virulent in character, the child dying, despite the vigorous use of antitoxin. It had evidently had the disease several days before clinical symptoms were noted. No idea that the contagion would spread was then entertained, but on February 13 two more cases developed in children in the same ward, Ward G, and two days later a fourth-year student on duty as a clinical clerk in this ward was found infected with the characteristic organism. In a period of twenty-two days eight cases of the disease had thus made their appearance, five of them located in Ward G, three in children patients and two in individuals rendering assistance in the care of these patients.

This number of cases of diphtheria was by no means out of the ordinary, either for large general hospitals of the size of the Johns Hopkins or for this Hospital itself. We have always had an occasional Klebs-Loeffler infection and shall always expect such sporadic cases. We live in a community where diphtheria is ever present, and the extension of the outside infection to the Hospital is never unexpected, nor is it usually a matter of concern. But when the Clinical Clerk on Ward G was found with the disease, and it was realized that three other cases had developed in the children on the same ward, it was suspected that the infection might have spread and a more or less systematic examination of patients, nurses and students in this ward was carried out. No cases were then brought to light, but four days later another fourth-year student in Ward G was found infected. This was on February 20, and on the following day diphtheria was discovered in three adult patients in Ward G, in three nurses in this ward, in another nurse, a room-mate of one of the infected Ward G nurses, and in a nurse in the general operating room, who had handled Ward G patients.

This more or less sudden outbreak of diphtheria in Ward G, or rather this sudden spread of the contagion, was viewed with great uneasiness by the medical internes and especially by the Resident Physician, Dr. Sladen, and by Dr. Austrian, who had been examining the cultures. The occurrence on one day of eight cases of diphtheria associated with one ward indicated a firmly seated focus of infection and a by no means remote possibility that this infection would spread in a number of directions. The very free access to the wards which our students enjoy added to the body of patients, doctors, nurses and attendants who might become infected, another fairly large and somewhat widely distributed group of individuals who could carry infection to various points. Actuated by a well justified concern, on February 21, after these eight cases of diphtheria were discovered, the Resident Medical Staff instituted a systematic examination of the hospital population. The throats of all were carefully studied for local signs of infection, and on the slightest appearance of suspicious symptoms the individuals were segregated and cultures taken. The following day three more cases of diphtheria were brought to light, an adult patient, a nurse in Ward G and a medical interne in another ward. On Thursday, February 23, seven cases were discovered, two more children in Ward G, three nurses and a member of the second-year medical class. On Friday, February 24, eleven cases of diphtheria made their appearance, two more nurses, a patient in Ward F and eight medical students.

At this time the situation was regarded as extremely serious by all the men who were working on the wards. Cases of the disease were cropping out with great rapidity and in a number of different areas. It was evident that diphtheria had gotten a firm foothold in the institution. From January 25 to February 25 thirty-eight cases had developed. This was despite the fact that the cases were recognized early, the diagnosis established soon after the appearance of clinical symptoms, complete isolation of all the patients carried out and energetic cleaning and disinfection employed to rid the infected localities of the contagious material. In brief, all the measures which under ordinary circumstances are employed to prevent the spread of the Klebs-Loeffler bacillus had been adopted and yet the disease was steadily increasing in intensity. The occurrence on two days of eighteen cases of diphtheria was too serious a matter for both the Hospital and the

* Paper read at the 1911 meeting of the Interurban Clinical Society.

Medical School not to be regarded with considerable uneasiness. It was furthermore clear that the disease was spreading in two directions, independently and simultaneously: first, in the group of persons associated with Ward G, patients, nurses and assistants, and individuals in the Nurses' Home, who had been in contact with the Ward G nurses; and, secondly, in the student-body of the Medical School. In regard to the first group of people two possibilities existed, one that a focus of diphtheria existed in Ward G, from which source it spread to the Nurses' Home, the other that a focus existed in the Nurses' Home, from which point it spread to the patients in the ward. In the second group, the medical students, cases had been discovered in all the classes and the appearance of a greater number in the first- and second-year students, who do not come into the hospital, than in members of the third- and fourth-year classes, who might be infected from ward cases, was a proof of the independent transmission of the disease among the students themselves. Various avenues by means of which the infection might be spreading in the student-body were suggested, the most probable channels being the Lunch Room in the basement of the Physiological Building, where about a hundred men and women from all four classes take their midday meal, and the various students' clubs and boarding houses.

At the meeting of the Advisory Board of the Medical Faculty on Friday, February 24, the many details of the situation were presented by Dr. Barker, and it was decided to close the Medical School. A committee was appointed to take charge of the situation. This committee, known afterwards as the Diphtheria Committee, consisted of Dr. Williams, Dr. Barker and Dr. Ford. Dr. Norton was asked to become an ex-officio member as the Acting Superintendent of the Hospital. It should be mentioned that only by the active and willing co-operation of Dr. Norton with this committee was it possible to carry out the various measures which were suggested to stamp out the disease. To the Diphtheria Committee all questions relative to the epidemic in both Hospital and Medical School were referred.

On Saturday morning, February 25, Dr. Williams, the Dean of the Medical School, posted notices stating that the institution was closed temporarily. Later notices were sent to all the students urging them to remain in Baltimore, to keep in close touch with the school authorities and to avoid appearance in public places like theaters and churches. On the same morning the Diphtheria Committee held its first meeting. The various features of the epidemic were discussed at length and certain general measures were decided upon. These measures included the further examination of all the Hospital inmates, patients, doctors, nurses, orderlies, etc., the taking of routine throat cultures from all the medical students, and the cleaning and disinfection of the medical buildings. An investigation into the conditions of the many boarding houses where the students live, to bring to light any hidden foci of infection, was also considered advisable, and Dr. W. L. Moss was asked to undertake this latter work.

At this time it was deemed of great importance to get in close touch with the Department of Health of the City of Baltimore, and Dr. Moss and Dr. Ford, at the request of the committee, had a long conference with Dr. Jones, Assistant Commissioner of Health. At this conference a number of plans of work were considered. Dr. Jones suggested at once the importance of taking throat cultures from all the inmates of the students' boarding houses to determine whether the infection was spreading or likely to spread to the city. He put the resources of the Health Department at the service of Dr. Moss in his investigation and made him a temporary official of the Department. Dr. Jones expressed his great desire to co-operate with the Diphtheria Committee in any way possible, and all questions affecting the relationship of the Hospital and the city, such as the discharge of patients, were thereafter submitted to him for decision.

On Saturday, February 26, six additional cases of diphtheria developed and on the following Sunday eight more, three in members of the Faculty or their families. When the committee met on Monday fourteen cases had thus been added to the thirty-eight already reported, making a total of fifty-two. It was evident that the disease was spreading rapidly and it was therefore decided to close the Dispensary, partly in order to give it a thorough overhauling, and to admit no more patients to the Hospital except certain urgent cases who were to be warned of the danger.

By this time the various measures of cleaning and disinfection, of taking routine cultures from the throats of the Hospital and Medical School population, the complete isolation of individuals with positive throat cultures, the detention of suspects, had been put in operation. It was apparent that some of the patients were rapidly recovering and would soon be ready for discharge. A number of non-infected patients were also anxious to leave the Hospital. Dr. Jones was therefore appealed to, for a ruling in regard to the matter. He decided that the patients should be divided into three groups and treated as follows: First, all persons who had recovered from diphtheria could be discharged when two negative cultures from nose and throat separated by a forty-eight hour interval had been obtained. Secondly, all persons exposed to diphtheria and not contracting the disease could be discharged when one negative nose and throat culture had been obtained. Thirdly, all persons not exposed to the disease could leave when one negative throat culture had been secured. Acting upon these rulings on Tuesday, February 28, Dr. Norton posted notices in the Hospital and began the discharge of patients.

The cleaning and disinfection of the Medical Building was put in charge of the writer and presented a special problem which may be considered briefly. The buildings are large, divided into many rooms, devoted to all sorts of purposes, and were in active use at the time of closure. The presence of large corridors and stairways, establishing a free communication often between basement and attic seemed to render any gaseous fumigation valueless. Largely upon the advice of Dr.

Jones, it was decided to disinfect with formaldehyde wherever possible, but to rely mainly upon a thorough cleansing of the floors and walls to a height of about six feet, after the buildings had been allowed to rest absolutely undisturbed for 24 to 48 hours to allow the dust to settle. Attempts which were made to disinfect some of the rooms with formaldehyde gas obtained from such preparations as briquets of formanganate and patent candles which on burning evolve this vapor, demonstrated the uselessness of the procedure. In a few minutes after the evolution of the gas had been brought about the odor of it had disappeared from the rooms, the many openings about the doors and windows, the heating apparatus, and the ventilating shafts, permitting it to pass into other parts of the building. It was evident that some method of obtaining a continuous evolution of the gas lasting a number of hours must be hit upon if an effective disinfection of these large buildings was to be obtained. At the suggestion of Mr. Hartley, head janitor of the Anatomical Laboratory, this object was accomplished by the long-continued boiling of solutions of 40% formalin in water in the proportion of about one part to three. The windows and doors of the buildings were tightly closed, all the inside doors leading from the rooms to the corridors opened and saucepans containing the formalin mixture were boiled over Bunsen burners in a number of different localities. A constant evolution of the gas lasting six to eight hours was thus obtained, the atmosphere of the building being saturated with the vapor for a considerable period of time. The flames of the Bunsen burners were extinguished by turning off the main supply of gas in the basement and on the following day the buildings were opened, thoroughly aired and the work of cleaning undertaken. The floors and walls were first washed with soap and water and then wiped off with some disinfectant solution, either a solution of carbolic acid or one of corrosive sublimate. Whenever the latter substance was used it was followed by another washing with soap and water.

In buildings where the presence of animals or expensive apparatus likely to be injured by the vapor of formaldehyde prevented this disinfection of the structure as a whole, the separate rooms were sealed up and fumigated by the Parke Davis formanganate briquets or by the Du Prey candles. These rooms were kept tightly closed for 24 hours and then the floors and walls were washed with soap and water and with disinfectants.

No bacteriological tests were made to determine the efficiency of the fumigation. The necessity for rapid work precluded any satisfactory observations, and it was realized that no method of disinfection is perfect. It was decided to carry out as vigorously as possible those methods which are recognized to be of the greatest value and to trust to a wise providence that the contagion would be destroyed. Afterwards, when more time was available, with Dr. Norton's help, a number of observations were made during the disinfection of Ward G. It was found that surface cultures of organisms like *Bacillus typhosus, Bacillus coli, Streptococcus pyogenes, and Bacillus prodigiosus* were killed when exposed to the gas generated by the Parke Davis briquets of formanganate. The organisms in the depths of the tubes remained viable however.

Special emphasis was placed upon the disinfection and cleaning of the Lunch Room in the basement of the Physiological Laboratory. From the beginning of the epidemic it was believed that it might be one of the main foci of infection among the students. Primarily it was the only place where there was a general meeting of the members of all classes. Again, certain practices in vogue there, such as cleaning the table-tops with napkins left by students who had already taken their lunch and departed, seemed to offer an abundant opportunity for the spread of any contagious material coming from the throat. This room was therefore fumigated and washed thoroughly on two occasions separated by an interval of several days, and when finally reopened certain changes were instituted in the care of the dishes and napkins.

The students were encouraged to disinfect their own rooms, and in many instances were supplied with material from a quantity of disinfectant which had been sent to the school from the Department of Health. In all the students' clubhouses and in the majority of students' boarding houses this procedure was carried out most energetically.

Certain special difficulties were met with in the work of cleaning. In the first place it was extremely hard to get labor because of the widespread fear of diphtheria which had been engendered in the minds of the various residents in the vicinity of the Hospital, partly because of the wide publicity which had been given the epidemic by the newspaper reports. In the second place it was believed that all the people working in the buildings would be exposed to infection with the Klebs-Loeffler bacillus and the problem of their proper care had to be met. Eventually, a sufficient number of active people were obtained to do the necessary work. No cultures were taken from the throats of these individuals during their time of employment. It was perfectly evident that if suspicion should arise that they stood in danger of infection under no circumstances could they be induced to remain at work. At the same time it was realized that these individuals should be carefully examined at the end of the period of cleaning and disinfection to determine whether any of them had become infected with the diphtheria bacillus. This work in the medical buildings was completed in about a week from the time it was started. On Saturday, March 4, cultures were taken from all the workpeople, the extra employees were discharged, and the control of the buildings turned over to the Dean of the school. One positive throat culture was found in a woman who had been working in the Physiological Laboratory. It was not absolutely certain that this woman became infected in this building, since we had no negative throat culture at the time she began her work there, but the presumption was in favor of this source of her contagion. This case proved to be of considerable interest and importance. The woman harbored diphtheria bacilli in her throat for a period of fully 20 days, during which time she had no clinical symptoms or signs whatever. All sorts of measures were carried out to rid her throat of the organisms, such as spraying with various disinfectants and

with antitoxin itself. She received as well the regular antitoxin treatment administered subcutaneously. Eventually two negative cultures from her throat were obtained by the officials of the Health Department, and she was discharged from quarantine. This was one of the few definite cases in this epidemic where the diphtheria bacillus remained for some time in the throat of an individual without causing the appearance of clinical symptoms.

The most perplexing question which the Diphtheria Committee had to decide was in regard to the use of prophylactic or immunizing doses of diphtheria antitoxin. This measure was discussed on a number of occasions. A large number, if not all, of the doctors and nurses in contact with the disease took this treatment soon after the epidemic broke out. It was a matter of great importance, however, to determine whether this procedure should be insisted upon with all the inmates of the Nurses' Home and with the members of the Resident Staff of the Hospital. The Health Department from the first had recommended prophylactic antitoxin as the only remedy which could be relied upon to stop the spread of diphtheria among the nurses. At the same time the administration of antitoxin is certainly followed in a few individuals by the appearance of disagreeable or untoward consequences and authorities are by no means agreed as to its value in checking epidemics. Relying upon several experiences in Baltimore where diphtheria has been stamped out of a number of institutions only when prophylactic antitoxin has been administered to all the inmates, upon reports from various hospitals for the care of contagious diseases in which this treatment is carried out as a routine measure with the children when diphtheria appears, and upon a number of publications as to the percentage of bad results which follow the use of antitoxin, the committee decided to recommend but not to insist upon this measure. Whenever antitoxin had been administered previously, wherever an authentic history of attacks of asthma could be elicited, contra-indications were recognized to the use of the remedy.

A careful record of the administrations of antitoxin was kept by Dr. Sladen and his staff. Over three hundred prophylactic doses were given, two hundred nurses receiving the treatment, forty-three students, and a small proportion of the resident staff. About seventy patients took curative doses of the remedy. Nearly all the individuals who received the antitoxin either for prophylactic purposes or to combat an existing infection with the Klebs-Loeffler bacillus developed some local signs. In most cases the reaction was limited to slight urticaria. In a few instances a pronounced œdema was noted with local tenderness and elevation of temperature in the dependent parts near the site of injection. In five cases characteristic serum disease appeared. In one of these cases, a fourth-year student, immediately following the injection of the antitoxin a typical anaphylactic shock developed with great dyspnœa, shivering, vomiting, and attacks of faintness with tendency to syncope. These symptoms lasted for a number of hours but eventually entirely disappeared. This student had received antitoxin previously and gave a history of asthmatic attacks in his youth. In the other four cases in but one or two instances had antitoxin been administered previously.

How far the prophylactic use of diphtheria antitoxin was instrumental in stopping this epidemic is not clear. A number of interesting facts were noted which indicate that its use did have a definite effect upon the spread of the disease. The only nurse in Ward G who refused antitoxin later developed diphtheria. Among the other nurses on this ward who received the treatment no cases of infection appeared. Of the six children in Ward G, all exposed to infection, four received prophylactic antitoxin. Of these four, two later showed positive cultures of the diphtheria bacillus, but had no serious symptoms. The two other children on Ward G, in whom it was not considered advisable to administer the antitoxin because of recent surgical operations, developed diphtheria later and died. Coincidently with or immediately following the general administration of prophylactic doses of antitoxin to the nurses in the Nurses' Home, the infection disappeared in this group of individuals, and it did not disappear until this measure was carried out. While thus no proof can be brought to show that this procedure was operative in controlling the infection, the majority of the men who administered the antitoxin and followed the cases of diphtheria afterwards were convinced that it had no little influence in checking the epidemic. At the same time the prophylactic use of diphtheria antitoxin is probably the one measure adopted which might not be carried out so vigorously should we have epidemics of diphtheria to deal with in the future. While in our experience no serious results developed from the use of this remedy, there is a very general sentiment against it in both doctors and nurses, and this feeling is undoubtedly justified by the observations which have been published.

On Friday, March 3, it was apparent that the epidemic was dying out. From a case incidence of eight on the preceding Sunday, the number of cases had dropped irregularly during this week. Two cases in the nurses appeared on Monday, no cases were reported on Tuesday, three were found among the students on Wednesday, four cases developed on Thursday, one student, one nurse, one ward doctor and one orderly, and two came to light on Friday among the laundry employees. Altogether but eleven had developed in five days, and these had such a varied distribution as to indicate that they were but scattering cases at the end of a general epidemic. On Friday, therefore, Dr. Williams sent notices to the students and instructors that the school would open again to the first two years on Wednesday, March 8; to the last two years on the following day, at which time the dispensary was to be opened again to the public. Cultures were taken from all the students and instructors and only those with negative reports admitted to the school. The exercises began again on Wednesday and by the latter part of the week the routine of the Medical School had been re-established in all the classes. The infected wards of the Hospital were cleaned and fumigated, the patients who had recovered were discharged and new patients again were received for treatment.

A few cases of diphtheria did show themselves after Friday, March 3, at which time it was thought that the epidemic was over and the decision to reopen the school was reached. Thus on March 6 a child in the Maternity Ward was found with a positive nose culture, on March 7 a student developed a positive throat culture, on March 16 another student showed the infection, and on March 19 one of the physicians in the dispensary. On March 22 the room-mate of the last-named student developed an otitis media which proved to be due to the Klebs-Loeffler bacillus. Since that time no cases have appeared either in the student-body or among the individuals living in the institution. Altogether 66 cases of diphtheria were treated in the Johns Hopkins Hospital, to which should be added 6 cases in orderlies or members of their families who for various reasons could not be treated in the Hospital but who evidently contracted the disease there, a total of 72 cases. Four deaths occurred, three in children and one in an adult, none of them, however, being uncomplicated diphtheria cases.

We shall probably never know the source of this epidemic of diphtheria. Baltimore always has cases of the disease, and at times during the winter season these cases may occur with some frequency. From these foci of infection in the city the disease frequently extends into the Hospital, but at no time previously has there been evidence of any wide invasion of the Hospital population, nor has the fear been felt that such an invasion was likely to occur. In the three and a third years from September 1, 1907, to January 1, 1911, there have been but forty-four diphtheria patients in the Hospital. These cases occurred in individuals living in widely separated parts of the city, of various ages and occupations. Occasionally several cases have developed on or about the same time among the nurses or among the medical students. Thus in May, 1908, there were 5 cases of this description. The infection died out but during the next winter a few scattering cases appeared in the Hospital inmates. In the year 1909 there were about eighteen cases of diphtheria admitted to the Isolation Ward, of whom six were in the Hospital population and two among the medical students. In 1910 there were altogether eleven cases, of whom four were nurses or pupil nurses in the Hospital. These cases occurred at longer or shorter intervals, and while they may have developed one from another, they may equally well have been simply extensions of the disease from the city. At no time was there any difficulty in controlling these infections, and at no time was there any fear that the disease would spread in our midst. This sense of security was rudely shaken by our recent experience, and the possibility that an infection of mild form and almost self-limited may at times assume the character of a rapidly spreading contagious disease will always be entertained here in the future.

Finally, the question arises as to whether the very drastic measures adopted to stamp out this epidemic were necessary and whether the cessation of cases was directly due to the introduction of these procedures. Such questions from their very nature cannot be answered. We can only say that at the time the measures were put in operation, diphtheria was spreading with great rapidity in the Hospital and Medical School. All the men intimately associated with the work, especially the members of the resident medical staff, were appalled at the way the cases were coming to light and it was generally believed that unless drastic measures were employed a widespreading and serious epidemic of diphtheria might develop in the institution. With the inauguration of the various preventive methods which were considered advisable the disease disappeared from our population, and we cannot help but believe that this disappearance stands towards our activities in the relation of effect and cause and not in the relation of a sequence of events.

INFECTION OF THE URINARY TRACT BY THE BACILLUS LACTIS AEROGENES, WITH A CONSIDERATION OF THE MODE OF ENTRANCE OF BACTERIA INTO THE BLADDER.

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Following the introduction of exact bacteriological methods by Koch, there appeared, in addition to descriptions of morphology and motility, more or less accurate descriptions of the cultural characteristics of the bacteria found in cystitis.

From 1887 until 1892 a series of observations were made by French authors who found, in cystitis in man, a bacillus as the most frequent cause of cystitis. This bacillus appeared under various names. Morelle [1] and Denys [2] identified it as the *B. lactis aerogenes;* while it was later definitely proven to be none other than the *B. coli communis* by Achard and Renault,[3] Reblaud,[4] Krogius,[5] and later observers. Were it not for the fact that these early observations are still classed under the *B. lactis aerogenes,*[6] I should hesitate to give a more extended historical review.

A careful study of the originals in the light of present-day knowledge should leave no doubt as to the exact identity of this particular bacillus.

In 1887 Clado [7] isolated the "bactérie septique de la vessie," stating that this bacillus had not been described by any one.

This bacillus had rounded ends, and was actively motile ("movements of translation" as distinguished from "movements of place"); it travelled rather rapidly, in some in-

stances across the field of the microscope, and did not stain by Gram's method. The colonies on plates had an irregular outline, and the agar slant had a thin, opalescent growth.

In 1888 Albarran and Halle[8] isolated the "bactérie pyogène" from 35 out of 50 pathological urines obtained aseptically from the bladder. This organism was found 15 times in pure culture, and 20 times associated with other organisms.

This bacillus was 4 to 6 μ long, with a diameter of 2 μ, had rounded ends, and was motile in young cultures, but did not stain by Gram's method. The colonies on plates had rounded borders, and looked like drops of wax. In the gelatine stick, the culture formed a white stem with a white hyaline layer on the surface. They concluded that their bacillus was the same as that described by Clado.

In 1889 Doyen[9] isolated from urine in cystitis 10 bacilli and 4 micrococci. Of the bacilli, 9 did not liquefy gelatine, nor had they any other characteristics to distinguish them from the "bactérie pyogène" of Halle and Albarran.

During the same year Rovsing[10] isolated the cocco-bacillus urea, from 3 of the 29 cases under observation. According to Schmidt and Aschoff[11] this bacillus was probably none other than the "bactérie pyogène" of Halle and Albarran.

In 1889 Morelle (loc. cit.) found a non-liquefying bacillus in 13 of 17 cases studied, of which 6 were in pure culture. This bacillus was small with rounded ends, sometimes ovoid, and very variable in length. Its size was always influenced by the media. The bacillus was possessed of "movements of translation." No spores were found. On agar the colonies were round, glassy, smooth, and if discrete, reached 4 mm. in size. When translucent, an exquisite design of concentric lines was often observed. He noted both the opaque and the translucent type, presenting a pleomorphism which would lead one to believe them to be different species. The growth on potatoes was white to yellow, and showed bubbles of gas. It coagulated milk in two days, with acid production. It fermented glucose, with formation of CO_2 and H.

He concluded that his bacillus was identical with (1) the "bactérie septique de la vessie" of Clado, (2) the "bactérie pyogène" of Albarran and Halle, (3) the cocco-bacillus urea of Rovsing, and probably with the 8 species described by Doyen.

After a careful comparison of the morphological and cultural properties, he concludes that his bacillus is none other than the *B. lactis aerogenes* of Escherich. In comparing it with the colon bacillus, he admitted that there was a great similarity, and that their pathogenic action was the same.

The differences cited were that the *B. lactis aerogenes* developed on gelatine into higher and more circumscribed colonies; with regular outlines; that they were white and more opaque, while the colon colonies were gray and translucent; also that the *B. lactis aerogenes* colonies were viscous, while those of the colon were more dry. He ends with the following sentence: "Still the similarity is great, and one may perhaps some day demonstrate that they are only two varieties of the same organism."

Achard and Renault (loc. cit.) were the first to call attention to the identity of the "bactérie pyogène" and the colon bacillus. They compared two strains obtained from Albarran and Halle, one strain obtained by Gilbert and Girode from the bowels of a new-born, and various strains obtained from cases of pyelonephritis. All had the same morphology, the same motility under similar conditions, and the same cultural characteristics. They also found the pathogenicity the same.

At the same time Reblaud (loc. cit.) reported his work of the previous year, from which he concluded that the "bactérie pyogène" is identical with the colon bacillus. Charrin[12] took the same view.

In 1892 Krogius (loc. cit.) examined 17 pathological urines from cases of cystitis, and in 12 found a small motile bacillus with rounded ends, and of very variable dimensions. The urine was acid, with a particularly fœtid odor. He compared this bacillus with the "bactérie pyogène" obtained from Albarran and Halle and found them identical. Injected into the bladder of rabbits, his bacillus produced the same symptoms of purulent cystitis as the "bactérie pyogène." He also found that by growing the opaque type in sterilized normal urine for several weeks, it was transformed into the transparent type.

Laruelle found that by growing the opaque form in milk it was changed into the transparent type. Krogius was able to confirm this result.

We have thus a bacillus termed variously the "bactérie septique de la vessie," "bactérie pyogène," cocco-bacillus urea, *B. lactis aerogenes, B. coli communis,* all possessing the same cultural characteristics and the same morphology, active motility, and causing cystitis in 71 per cent of the cases examined.

Two points should suffice to prove that these cultures could not have been the *B. lactis aerogenes:*

1. All were actively motile—"movements of translation."

2. They occurred in about 70 per cent of the cases of cystitis, which figures correspond closely to the percentage of cases of cystitis due to the colon bacillus as shown by all of the later investigators.

The differences in morphology and the cultural differences on gelatine are now known to be insufficient and too variable to differentiate them as separate species.

From this period on, one finds the colon bacillus as the causative agent of cystitis in 50 to 71 per cent of all cases of cystitis, while the *B. lactis aerogenes* has only rarely been found. A careful search of the available literature revealed only a few isolated reports.

In 1899 Warburg[13] reported a case of bacteriuria in a man 54 years old, who was admitted to the hospital for a slight bronchitis. On the fifth day after admission he had a chill, headache, and a rise in temperature to 39° C. The fever continued for three days, and on the second day the urine became cloudy. A catheterized specimen showed a small bacillus, often coccus-like, which was not motile. It did not stain by Gram's method. On gelatine the growth was nail-like; on potato whitish yellow; it coagulated milk in 12 hours; in sugar bouillon it produced gas; it produced no indol.

In 1894 Heyse[14] reported a case of pneumaturia in a patient who was 23 years old, and in her second month of pregnancy. She suffered from a "myelitis lumbalis ascendens," completely paralyzing the bladder and rectum, necessitating catheterization three to four times each day.

The urine was at first clear, acid, and free from albumen and sugar. On the fourth day after admission the urine became cloudy, containing pus and red cells. Four days later a tympanitic tumor reaching to the umbilicus was observed, and the urine finally became alkaline.

The following organisms were isolated: a coccus which liquefied gelatine, a non-liquefying coccus, and a non-liquefying bacillus. The last was identified as the *B. lactis aerogenes*, and held by him as the cause of the pneumaturia.

This bacillus had rounded ends, but was so often like coccus that doubts were entertained as to its purity until gelatine plates were made. The bacillus was not motile and did not stain by Gram's method. No spores were observed. The growth on potato was several millimeters thick, grayish white, viscous, moist, and shiny, showing numerous gas bubbles. The bouillon was uniformly cloudy, forming a sediment. Milk was coagulated in 24 hours. It fermented glucose and lactose. The gas consisted of 63 per cent CO_2, 27 per cent H, and 8 per cent "undetermined rest." These proportions of gas stamp it as a true *B. lactis aerogenes*, according to Burri and Düggeli.[15]

In 1901 Wildbolz[16] reported a case of pneumaturia in a man 52 years old who was suffering from a gonorrhœal stricture which had to be dilated. Three weeks later he noticed gas at the end of micturition. The urine was cloudy, acid, and had a disagreeable odor. A non-motile organism was isolated which did not stain by Gram's method. It coagulated milk rapidly, actively fermented grape sugar, but did not form indol.

In 1894 Schnitzler[17] reported a case of pneumaturia in a nullipara 46 years old. In the fall of 1893 she noticed the passing of gas at the end of micturition, but did not suffer from any other symptoms. On December 11, 1893, a cystitis developed and the patient was catheterized by a midwife, from which time on she had to be catheterized several times a day. A short, plump, non-motile bacillus was isolated from the urine. This bacillus did not stain by Gram's method. The growth on gelatine was profuse. It formed gas even on sugar-free media. No note is made as to growth on milk or potato, the fermentation of glucose and milk sugar, the formation of indol, or the presence of a capsule. His conclusion was that his organism belonged to the colon group. Adrian and Hamm think that in the light of present-day knowledge this bacillus really belonged to the lactis aerogenes group.

In 1896 Trumpp reported 29 cases of cystitis in children, one of which was due to the *B. lactis aerogenes*.

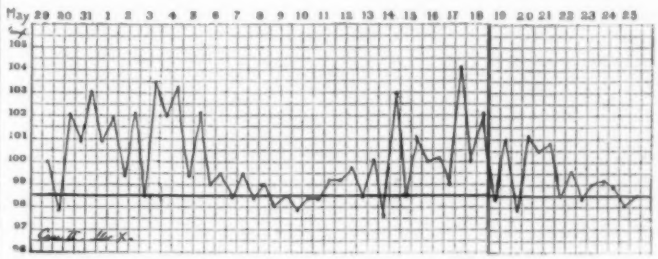
My personal observations were made on two cases with the following histories:

CASE I.—Mrs. X, aged 28, during the second month of first pregnancy complained of frequent micturition which direction as to diet, fluids, and rest did not relieve. The symptoms became aggravated with marked tenesmus, bearing-down pain, and great frequency of micturition. Her condition was such as to require rest in bed with a diet of milk and water, also suppositories of opium to relieve the straining. She had no pain in the region of the kidneys, and her temperature was never over 99° F. The urine was light yellow, acid, and contained a sediment consisting chiefly of leucocytes with an occasional red cell. Albumen and sugar were absent.

Bacteriological Findings.—Each of two catheterized specimens taken ten days apart showed the *B. lactis aerogenes* in pure culture. The condition persisted for four weeks with a marked tendency to recurrence whenever the urotropin was omitted. Later cultures were negative.

CASE II.—On May 25, four days after the acute symptoms in his wife had shown themselves, Mr. X, husband of Case I, developed a urethritis, accompanied with a yellowish, watery, acrid discharge which contained a few pus cells but no gonococci. He suffered from frequent micturition and a marked tenesmus requiring opium suppositories. The urethral discharge disappeared after the first day of rest in bed, on a diet of milk and water. The tenesmus and frequency of micturition also abated. The temperature, which was at first practically normal, after four days reached 103° F., as shown in the accompanying chart.

There was marked prostration, headache, and some nausea. These constitutional symptoms so overshadowed the local process



On June 9, fourteen days after onset, the temperature reached normal and remained so for two days, after which the patient began to complain of pain in the right abdominal region, extending into the inguinal ring on the following day. Twenty-four hours later a marked epididymitis had developed. The temperature reached 104° F., and the fever continued until June 26. The case terminated in a complete recovery with no recurrence.

that a blood culture was made on May 31, and a Widal test on June 3. In both, the results were negative. A physical examination revealed nothing. The prostate was not enlarged or tender. The urine was acid and cloudy, the last portions being especially turbid. At times a decidedly bloody tinge was noted. On microscopic examination, the sediment consisted entirely of leucocytes and red cells.

A bacteriological examination of the urine was made on the ninth and fourteenth day of the disease, and each time the *B. lactis aerogenes* was found in pure culture. The urine was obtained aseptically by means of a silk olive-tipped catheter, after previously irrigating the anterior urethra with a sterile boric acid solution.

CULTURAL CHARACTERISTICS OF ORGANISMS ISOLATED.

In the hanging drop, Brownian motions were observed, but never independent movements such as to change the relative positions of the organisms. Cultures of different ages were tried, always with the same results.

Some difficulty was experienced in determining whether we

were dealing with a coccus or a bacillus. Even in stained specimens there was doubt as to whether the culture was pure, until plates were made.

The organism was a small bacillus, with rounded ends; coccus forms were frequent. It did not stain by Gram's method. Capsules were readily demonstrated.

On agar plates, the colonies reached the size of one millimeter in diameter in 18 hours, and had a bluish opalescent appearance by transmitted light. Under the microscope, the colonies usually had a regular outline, while in some the borders showed slight undulations. They were translucent, with opaque and granular centers. The deep colonies were wedge-shaped and opaque.

The agar slants showed a bluish opalescent growth by transmitted light, one millimeter wide after 24 hours, and with raised edges.

On potato there was a heavy, yellowish white, viscous growth, several millimeters thick, rapidly covering the entire surface. The older cultures showed a deeper yellow color. No gas bubbles were observed.

Milk was coagulated in 24 hours with acid production.

Glucose agar stick cultures were much split up by the accumulated gas. In the fermentation tubes, saccharose solutions showed considerable gas production.

The morphology, capsule formation, absence of motility, rapid coagulation of milk, together with the gas production, leave no doubt as to the identity of the organism. The rapid coagulation of milk excludes the Friedlander bacillus."

Mode of Entrance of the Bacteria into the Bladder.

The bacteria may invade the urinary tract through the urethra, through the kidney, or from an adjacent abscess or other inflammatory process.

It is usually assumed that when there is no history of catheterization the infection must be an endogenous or descending one. There are two considerations which controvert this view:

1. The greater frequency of cystitis in women than in men, when there is no explanation of the mode of entrance of the bacteria into the bladder other than difference in sex.

2. The frequent existence of bacteriuria without infection of the ureters when no instruments have been introduced.

1. Relative frequency of cystitis in men and women in which there is no explanation of the mode of entrance of bacteria into the bladder other than difference in sex.

In general practice I have been impressed with the frequency with which one meets with cystitis in women, and the rarity of cystitis in men, if one excludes the cases due to gonorrhœa, tuberculosis, and diseases in which the bacteria are obtained by blood culture, such as typhoid, pneumonia, septicæmia, etc., and in those patients on whom instruments have been passed.

The gynecologist sees only women and the male genito-urinary specialist sees only men, so that neither has an opportunity to make a comparison. Nevertheless, the gynecologist must be impressed with the great number of cases of non-gonorrhœal cystitis in women who have never been catheterized; and the male genito-urinary specialist must be struck with the fact of the rarity of a non-gonorrhœal cystitis in the male who has never been catheterized, and who is free from any urethral or prostatic disease. A review of the histories of the large series of cases reported bears out this contention.

Of Rovsing's[19] 87 cases of bacteriuria and cystitis, 66 were male, and 21 female. Of the 66 male patients, definite mention of catheterization, fistula, or neighboring abscess was made in 51, or 88 per cent. Of the 15 remaining cases, one had phymosis; three had incontinence (one of which was due to tabes); five had retention due to stricture; and one an enlarged prostate. These therefore had a continuous column of urine through which the bacteria could readily have gained entrance. One case had pneumonia and another septicæmia, in both of which the organisms could probably have been obtained from the blood. This leaves only two cases, or 3 per cent, without sufficient explanation as to the mode of infection. Of these, one case was a boy 19 years of age with bacteriuria, who had renal infection, while the other was a man of 78 years with bacteriuria who had cancer of the kidney.

Of the 21 women, only 7, or 33 per cent, had been catheterized. In the remaining 14, or 66 per cent, the bacteria probably gained entrance through the short urethral tract. Of the latter, 3 were girls aged 6, 7, and 21 years respectively; 2 cases followed painful coitus; two suffered from slight constipation; one had a tumor of the bladder; three were women 76 years old who had never been catheterized; one had hematuria; one had a stone in the right kidney.

His cases of pyelitis without cystitis are even more convincing. Of 21 cases, 16 were women and 5 men; of the 5 men, 2 had been catheterized or treated locally; 1 had a large prostate with complete retention; in only 2 cases out of the 5, or 40 per cent, was there no explanation as to the cause of the infection.

Of the 16 cases in women, there were 15, or 93 per cent, without any explanation as to the mode of infection.

Of Melchior's[20] 35 cases, 20 were men and 15 women.

Of the 20 men, 16, or 80 per cent, had been catheterized; 1 had tuberculosis; 1 was an old man with a large prostate who had incontinence; another had a large prostate with complete retention. This would leave only one case, or 5 per cent, without explanation as to the mode of entrance of the bacteria into the bladder.

Of the 15 women, 7, or 46 per cent, had been catheterized; 1 had tuberculosis; another was suffering from a typhoid cystitis. This would leave 6, or 40 per cent, without explanation as to the mode of entrance.

Escherich[21] reported 7 cases of cystitis in children between the ages of 6 months and 9 years, all due to the colon bacillus. Since all occurred in girls, and since several had a mild vulvitis, he concluded that it was most probable the bacilli entered through the short urethral tract.

Trumpp[22] reported 29 cases of cystitis in children from Escherich's clinic, of whom 21 were girls and 8 boys.

Suter[23] reported 118 cases exclusive of tuberculosis and gonorrhœal cystitis. He considered 35 of these endogenous, and 83 ectogenous or instrumental. Of the 35 endogenous cases, 15 were men and 20 women.

Of the 15 men in whom the infection is supposed to have occurred by the endogenous or descending route, one had gonorrhœa, stricture, and hypospadia; one had gonorrhœa with a very narrow stricture; one had gonorrhœa and prostatitis; one had prostatitis and epididymitis; one had epididymitis, large prostate, and residual urine; one was cystoscoped, after which procedure a severe cystitis followed; one had a cystotomy performed two years before for hematuria. All of these should be considered as ectogenous. This would leave 8 cases in which the histories are not complete enough to determine the route of infection, and as Alsberg[24] has said, not one of which is convincing in regard to the endogenous route.

Of the 20 women, only 2 were catheterized, leaving 18, or 90 per cent, without explanation as to mode of entrance.

Of his 83 cases classed under the heading of instrumental infections, only 5 were women.

Thus in his total of 118 cases 93 were men, in 87 of whom the origin of their cystitis was ectogenous, leaving only 6, or 6.4 per cent, without explanation as to the mode of infection.

In Brown's[25] series of 24 cases of chronic cystitis in women, 10 had never been catheterized, leaving 41.6 per cent without explanation as to route of infection.

To show how frequently women are infected, Albeck[26] reports the following cases: Of 150 non-pregnant women, 13 per cent had an infection of the urinary tract; in 392 pregnant women, 17 per cent had an infection; in 392 puerperal women, 14 per cent had an infection.

In Alsberg's series of 126 pregnant women, 12 per cent had an infection of the urinary tract; in 203 puerperal women, 29 per cent had an infection; in 41 cases of abortion, 17 per cent had an infection.

To summarize: In 192 men with cystitis or pyelitis, only 21, or 10 per cent, were without explanation as to the mode of infection; while in 129 women, 81, or 62 per cent, were without explanation as to the route of infection.

If there is a difference in the two sexes, it must be a local and not a constitutional one, and we find a ready explanation in the short and often relaxed urethral tract of the female.

Bacteria in the Normal Female Urethra.

The bacteria usually causing cystitis are inhabitants of the female urethra, the percentage varying according to the character of the cases examined and the methods employed. The colon bacillus has been found by all observers in from 12 per cent to 66 per cent of the cases. Recently Alsberg has found this bacterium in 100 per cent of the cases. He selected six cases of pregnancy and examined the urethra each day for twelve days. By taking *several loops of the secretion*, and plating on Drigalski-Conradi media, he found the colon bacillus in each case; if only one loop was taken, the results were not constantly positive on the successive days. He concludes that the colon bacillus is a regular inhabitant of the female urethra.

The differences in results obtained by different observers are due to the methods used; some wiped the lower portions of the urethra with bichloride and did not wash away the excess, others simply wiped the meatus with sterile cotton. The findings were also proportional to the amount of material used. Some used the loop, others used the straight wire. In many the differences were due to the media and the exactitude of the bacteriological methods employed.

The staphylococcus albus and aureus were found by different observers in percentages varying from 14 per cent to 90 per cent.

The bacteria of the urethra enter the bladder in two ways: They are introduced with the catheter, or they may enter directly from the urethra.

Any one reviewing the histories of the cases thus far reported and the percentages of cystitis following catheterization, will be impressed with the fact that catheterization is a very serious procedure, especially when local conditions are present such as trauma following gynecological operations and labor, pressure due to tumors or pregnancy, prolapse, retention, or paralysis.

The invasion of the bladder by microorganisms in the urethra is probably much more frequent than is usually supposed. The recent work of Albeck and that of Alsberg, who found infections of the urinary tract in 12 per cent out of a total series of 500 cases, seem to confirm this view. If a careful bacteriological examination were made in every case with mild bladder symptoms, we should find an ever increasing number due to the invasion of bacteria. This direct invasion from the urethra is favored by retention and incontinence, which produce a continuous column of fluid.

Nor is the male urethra a bar to the exogenous invasion of bacteria. The gonococcus does not seem to have any difficulty in invading the urethra and bladder. If the cases of non-gonorrhœal urethritis were examined carefully and the etiology determined, we should probably find the cause to be the bacteria which usually cause cystitis. The staphylococcus, streptococcus, and a diplococcus were found by Eitner.[27] The staphylococcus, colon bacillus, and an unrecognized diplococcus were found by Hume[28] in 11 cases examined. Other organisms found were the pseudodiphtheria bacillus, influenza bacillus, and the Friedlander bacillus.

2. The frequent existence of bacteriuria without infection of the ureters in cases which have never been catheterized.

Those who adhere to the endogenous route of infection refer to the fact that pyelitis, which is usually due to the colon bacillus, often occurs without any demonstrable lesion in the bladder.

Albeck has shown that in 150 non-pregnant women 13.3 per cent had bacteriuria, in 70 per cent of whom the bacteriuria was due to the colon bacillus. To determine whether the ureters were also infected he selected 13 cases and catheterized both ureters; in 8 cases the urine was clear and sterile from both ureters; in 3 no organisms were found on coverslips, and only a few colonies were found on the plates, which

he concluded were accidental; in 2 only were the bacteria in great numbers. He justly concludes that in a great majority of the cases the infection originates in the bladder.

We know that the bladder is very resistant to infection, and that the mere introduction of the colon bacillus will not produce a cystitis. If, however, the urethra or ureter is tied, a cystitis or pyelitis develops. All that is necessary to convert a bacteriuria into a pyuria is a retention. Such a retention is often produced during the second half of pregnancy, due to pressure on the ureters. Stone, trauma, or any of the accessory causes named above will produce the same result. If the retention or trauma affects the kidney, and not the bladder, a pyelitis develops without a cystitis.

The pathological and bacteriological studies of Schmidt and Aschoff (loc. cit.) of 16 cases of pyelo-nephritis confirm this view. They found that a microscopic examination usually gave the clue as to the route of infection. Where this failed, the microscopic examination supplied the information. The process always followed the tubules, and was ascending.

The preceding review thus shows that an ascending infection is of very common occurrence in women, and is also possible in men, when no instruments have been introduced into the bladder.

In the two cases reported in this paper the infection was an ascending one. In Case I the infection was limited to the bladder, since there was no pain in the region of the kidney and since there was no fever. The congestion and pressure caused by the pregnancy supplied the accessory factors enabling the organisms to invade the bladder.

In Case II (the husband) the infection certainly was an ascending one, since the infection started with a urethritis and since there was no fever until the infection reached the bladder. His symptoms started four days after the *acute* symptoms in his wife had developed, and were more severe, due possibly to the increased virulence of the organism which had passed through an intermediary host. The epididymitis must have been caused by the same organism, and extended by continuity along the seminal ducts as shown by the sequence of the location of the pain, and the gradual rise of the temperature. This case is particularly interesting in that it shows definitely an ascending infection of the bladder in the male by an organism other than the gonococcus. The general impression seems to be that unless instruments have been introduced, the infection of the bladder in the male must be by the blood route.

As a summary of this review, the following conclusions may be drawn:

1. The *B. lactis aerogenes* is a rare cause of cystitis.

2. The great majority of infections are due indirectly to the introduction of instruments.

3. Infections of the bladder, in cases where no instruments have been introduced, are very frequent in women and rare in men.

4. In infections of the bladder in women, without a history of the introduction of instruments, the route of infection is usually an ascending one and due to the direct invasion of the bacteria from the urethra.

5. Such direct invasion of the bladder also occurs in the male, and probably much more frequently than is usually supposed.

6. The introduction of a catheter or instruments into the bladder is a very serious procedure, since it may produce a pyuria if the local conditions are favorable, or a bacteriuria which later may be converted into a pyuria when the local conditions become favorable.

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COMBINED ADENOCARCINOMA AND MIXED-CELLED SARCOMA OF THE OVARY.*

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The association of malignant epithelial and connective tissue tumors in the same organ is well known. Carcinoma and sarcoma have frequently been found associated in the uterus. Each process has, however, been well defined and sharply differentiated from the other. The combination of these two processes in a single tumor is seldom observed. Much interest has been manifested in this combination since the work of Ehrlich[1] and Apolant on the transplantation of carcinomatous tumors in rats. From a purely carcinomatous tumor, they were, by repeated transplantation, able to procure a mixed tumor of carcinoma and sarcoma, and finally a tumor showing pure sarcoma. Their findings have been corroborated in Bashford's[2] laboratory. To use Bashford's words: "During transplantation of a rather slow growing adenocarcinoma with a somewhat fibrous stroma, a sarcomatous interstitial tissue has appeared in several separate strains. This has outgrown the carcinomatous elements in subsequent generations and given rise to a pure spindle-cell sarcoma." Isolated cases showing these combined processes have been reported. In 1904 Nebesky[3] reported a case of adenocarcinoma of the body of the uterus, showing a stroma of mixed-cell sarcoma. Taylor,[4] in 1909, reported a case of adenocarcinoma of the thyroid gland with a stroma of mixed-cell sarcoma, the latter process being the more vigorous.

A careful search of the literature for such a tumor occurring in the ovary has been unsuccessful. It was therefore deemed of sufficient pathological importance and interest to report in detail the following case:

Miss S., white, aged 50. Admitted to the Church Home and Infirmary in the service of Dr. T. S. Cullen, November 11, 1909. For several months she has had a great deal of pelvic pain and for the past two months has had considerable dysuria, necessitating frequent catheterization.

On pelvic examination, the cervix was found to be forward, the uterus back, and there was considerable edema of the vaginal vault, together with some slight induration. The pelvis and lower abdomen were filled by a rather tender hard tumor mass. There was strong suspicion of malignancy, so an immediate exploratory operation was indicated.

Operation, November 13, 1909. When the patient was examined under ether it was deemed advisable to do a pelvic puncture. A considerable quantity of free fluid and a great deal of blood were obtained, but there was no diminution in size of the tumor mass. The abdomen was at once opened and the large mass felt on ether examination found to be a malignant growth of the left ovary. The bladder was drawn high up over the tumor and adherent to the posterior surface; thus accounting for the dysuria and the necessity for catheterization. The tumor, together with the uterus and appendages from the opposite side, was removed as rapidly as possible. During removal it was found that the right ureter was densely adherent to the tumor and there was involvement of the peritoneum in the right side of the pelvis. The right ureter was dissected free by splitting the anterior part of the broad ligament, which enabled the operator to expose the ureter with considerable ease. Fully one-third of the pelvic peritoneum was removed with the tumor, and as far as could be seen macroscopically, no malignant tissue was left. An iodoform drain was placed down through the pelvis.

The patient made an uneventful convalescence.

GYN. PATH. No. 14414. *Pathological Report.*—The specimen consists of a uterus which has been removed supravaginally, together with a mutilated mass of tissue representing the appendages from the right side and a solid tumor of the ovary from the left side. Attached to the tumor is the left tube.

The uterus, apart from adhesions laterally, shows nothing abnormal. The right tube and ovary are bound in adhesions and the ovary is cystic. Fig. 1.)

The ovarian tumor in its present flattened condition measures 15 x 14 x 7 cm. It is generally smooth on the surface but in a few places old tags of adhesions are present. It has been attached by a pedicle about 3 cm. in diameter. Coursing over the tumor and attached to it by thin mesosalpinx is a tube, which has been converted into a hydrosalpinx. The surface of the ovarian tumor is somewhat irregular and nodular. It is greyish-yellow in color and numerous congested vessels are visible upon the surface. These vessels are most prominent in the valleys between the slightly nodular elevations. On section the tumor is found to contain a central shallow cavity measuring 5 x 9 cm., and at one point near the periphery it reaches a depth of 2 cm. (Fig. 2.) The floor of this cavity is smooth and is lined by a thin yellowish-white fibrillated membrane. It resembles very much a markedly enlarged kidney pelvis. Surrounding the cavity and occupying the space between it and the cortex are irregular lobulated areas which are greyish-yellow in color and in places present a finely granular honey-combed appearance. (Fig. 2, *a.*) In some places distinct hemorrhagic areas are visible and in others there is simply a brownish coloration of the tissue. At other points about the periphery are irregular firm whitish areas varying from 8 mm. to 2 cm. in diameter. (Fig. 2, *c, g, e.*) In some places these areas show evidence of breaking down with slight cystic formation. The picture presented is a distinctly malignant one. In some places the tissue appears carcinomatous, in others it resembles sarcoma.

GYN. PATH. No. 14414. *Microscopic Examination.*—Sections were taken from eight different portions of the tumor, representing every gross type of pathological process present. The tumor is found to consist of a well-defined adenocarcinomatous process and an equally well-defined sarcomatous one. In certain parts of the tumor these two processes are side by side. In others there is pure sarcoma with absence of any carcinoma. In still other parts are found areas where there is well-defined carcinoma and a rather cellular and suspicious looking stroma; the stroma, however, not showing the typical picture of sarcoma seen elsewhere. In those sections showing the combined processes, the

* A report of the original tumor was made before the Johns Hopkins Hospital Medical Society April 18, 1910.

[1] Ehrlich, P., and Apolant, H.: Berl. klin. Wchnschr., 1905, XLII, 871.

[2] Bashford and Haaland: Imperial Cancer Research Fund. (Third scientific report.) London, 1908, 248.

[3] Nebesky: Arch. f. Gynäk., 1904, LXXIII, 653.

[4] Taylor: J. Path. and Bacteriol., 1908, XII, 440.

carcinomatous one is marked by large islands of glands (Fig. 3), the glands in most instances being irregular in size and shape and presenting a distinctly atypical appearance (Fig. 4). The individual cells vary in size, shape, and staining qualities, and many nuclear figures are visible. Immediately adjacent to these islands of glands, the stroma shows a distinctly malignant appearance. The predominating cells are spindle-shaped and round, but there are many large irregular, deeply staining cells scattered throughout (Figs. 3 and 4, *d*). Some parts of the tumor show a greater number of these large cells than do others. The individual stroma cells vary in size and shape. The nuclei are as a rule large, stain rather deeply, and assume an oval or round contour. The protoplasm of the cells takes a fairly uniform stain. The large (atypical giant) cells assume different sizes and shapes. (Figs. 3 and 4, *d*.) The nuclei are irregular in outline, multiple, very deeply stained, and are surrounded by a considerable quantity of protoplasm. A number of nuclear figures are visible. The carcinomatous and sarcomatous processes are entirely distinct and independent and this point is especially well emphasized by the fact that the glands of the carcinoma have retracted from the stroma and there is a distinct area of separation between the two. The cells which line the narrow spaces that separate the carcinomatous from the sarcomatous processes are in the main uniform in appearance and seem to form a distinct membrane. In some portions of the tumor there is marked degeneration. Here the tissue has undergone extensive hyaline change and merely shadows of cells are present. Sections taken through the periphery show a well-defined capsule, which has undergone partial hyaline degeneration, and considerable infiltration with round cells. At no point was there evidence of penetration by either malignant process. The vascularity of the tumor, while not especially prominent, is in greater evidence where the sarcomatous process is most active.

The right ovary on microscopic examination shows no evidence of malignancy. Both tubes show some chronic inflammation, but there is no involvement by the malignant process. Sections from the body of the uterus show an early diffuse adenomyoma. The cervix is quite normal.

From the tumor it is impossible to determine whether one process preceded the other or whether the development was simultaneous. It is significant, however, that in those areas where the carcinomatous elements show the greatest disintegration the sarcomatous process presents a wilder and a more rapidly growing appearance. Degeneration seems to play some rôle in the early development of sarcoma in certain instances. This point has been emphasized by Kelly and Cullen[1] in their examination of myomata which have undergone sarcomatous transformation. In many instances the sarcomatous tissue was adjacent to hyaline degeneration on the one side, and fairly typical looking myomatous tissue on the other. Bashford (*loc. cit.*) states: "In all the latter stages of sarcoma development we find the first changes beginning in the center of the carcinomatous tumor where sclerotic changes are present."

RECURRENCE OF TUMOR IN PELVIS.

Within a few weeks after leaving the hospital, there were signs of a recurrence of the tumor in the pelvis and the patient died on October 27, 1910, eleven months after the operation.

Autopsy Report.—(The body had been embalmed with a weak formalin solution about ten hours before the post mortem examination.) The body is markedly emaciated and the skin shows a diffuse yellowish tinge. There is some abdominal distension, due partially to fluid, but no edema of the extremities is present. On opening the abdominal cavity, there is found to be some distension of the bowel and about one liter of free fluid, with a distinctly formalin odor. The viscera have been partially hardened. Occupying the pelvis is a large semi-cystic mass which is intimately adherent to the sigmoid, rectum, bladder and pelvic wall. Scattered everywhere over the surface of the large and small bowel are numerous firm whitish nodules varying in diameter from 1 mm. to large confluent patches approximately 7 cm. in diameter. Sections through the affected portion of the bowel show the process to be limited to the outer coat. The omentum is markedly thickened and is studded with numerous large and small firm white nodules, similar to those on the bowel surface. The liver, spleen and kidneys are slightly enlarged, but show no evidence of metastases. Both lungs are edematous and a few scattered areas of broncho-pneumonia are present. Careful examination showed no evidence of metastases outside of the peritoneal cavity, no enlarged retroperitoneal glands were found.

Anatomical Diagnosis.—Pelvic tumor, general peritoneal metastases, broncho-pneumonia.

Gyn. Path. No. 15613. *Pathological Report.*—The tumor mass measures approximately 15 x 12 x 12 cm. It is cystic in character and is covered by many old adhesions. On section are found numerous cystic spaces, the largest of which is approximately 8 cm. in diameter. These contain some light straw-colored fluid and are lined by a shaggy tissue which is readily peeled off. The walls, which vary in thickness from 0. 5 to 5 cm., consist of a moderately soft homogeneous tissue, pinkish-white in color, closely simulating sarcoma.

Histological Examination.—As in the original tumor the two processes are combined, but the sarcomatous elements predominate. Scattered throughout a bed of sarcomatous tissue are groups of glands presenting the typical picture of adenocarcinoma (Fig. 5). The sarcoma belongs to the mixed-cell type, the spindle cells predominating. Numerous large, so-called giant cells, are present. These are well seen in Fig. 6. In some sections the picture was one of pure sarcoma, no glands being visible (Fig. 6). The metastases on the bowel wall and in the omentum show a picture of adenocarcinoma (Fig. 7). The stroma shows no evidence whatever of sarcoma.

Study of the original tumor shows a combination of the two malignant processes, the carcinomatous elements predominating. In the recurrent tumor, however, the process is mainly sarcomatous in character.

It is interesting to note that metastases were purely carcinomatous. They were limited to the peritoneal surfaces of the bowel and the omentum, simulating in great measure the picture observed in malignant papillocystomata of the ovary with general peritoneal implantations.

I am indebted to my brother, Dr. Thomas S. Cullen, for the privilege of reporting this case and to Dr. J. S. Bloodgood and Mr. Schapiro for the protomicrographs.

The patient was referred to Dr. Cullen by Dr. Clara Eirley, of Hagerstown, Md.

DESCRIPTION OF FIGURES.

Fig. 1. —Gyn. Path. No. 14414 (natural size). This picture represents the appearance of the ovarian tumor which has been hardened in 10 per cent formalin.

Fig. 2.—Gyn. Path. No. 14414 (natural size). On section of the tumor various stages of cystic and hyaline degeneration are visible. *b* represents a large central cavity lined by a slightly

[1] Kelly-Cullen. Myomata of the Uterus. W. B. Saunders Co., 1909, 175.

FIG. 1.

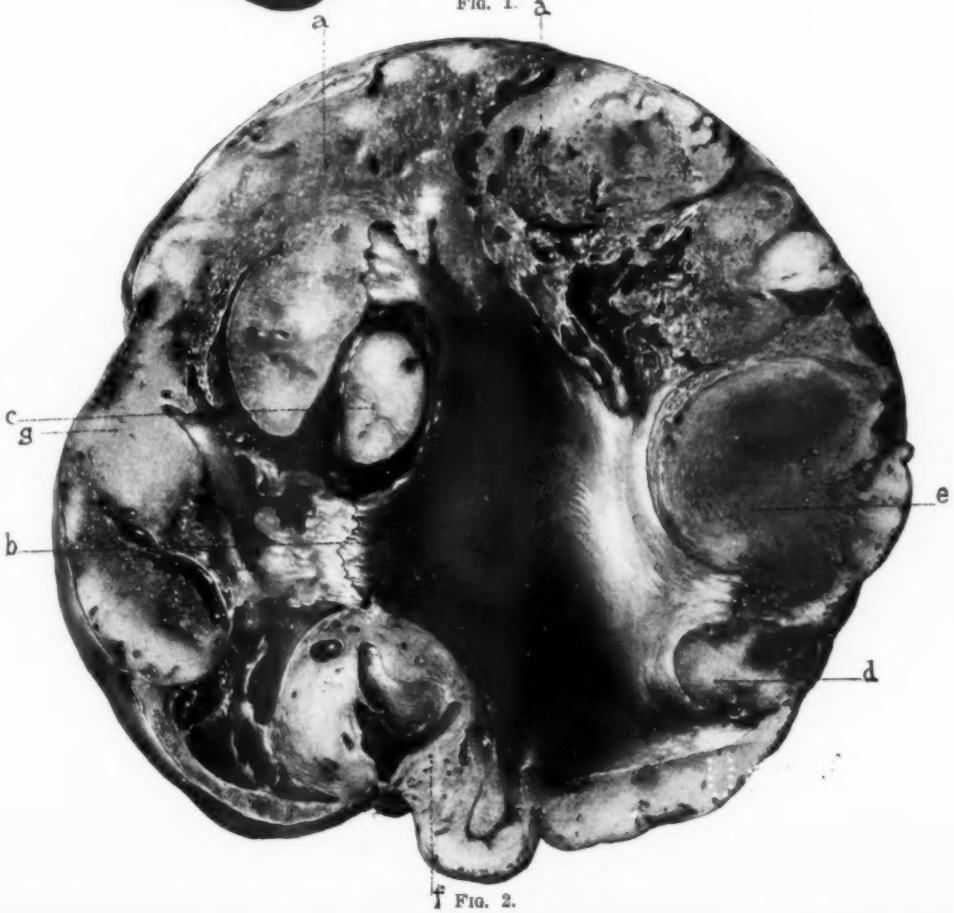

FIG. 2.

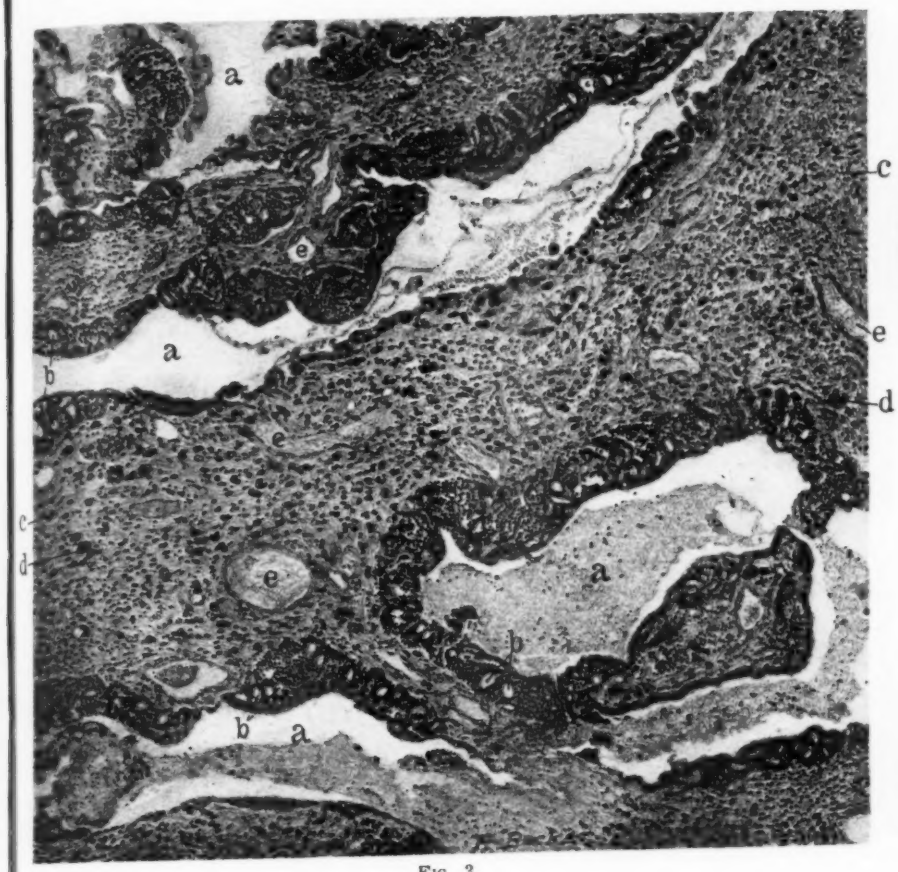

FIG. 3.

FIG. 5.

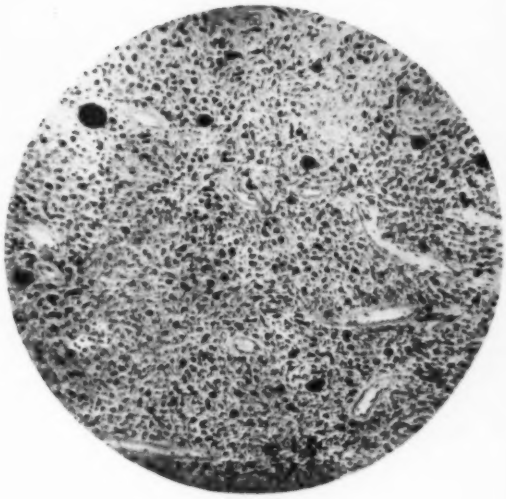

FIG. 6.

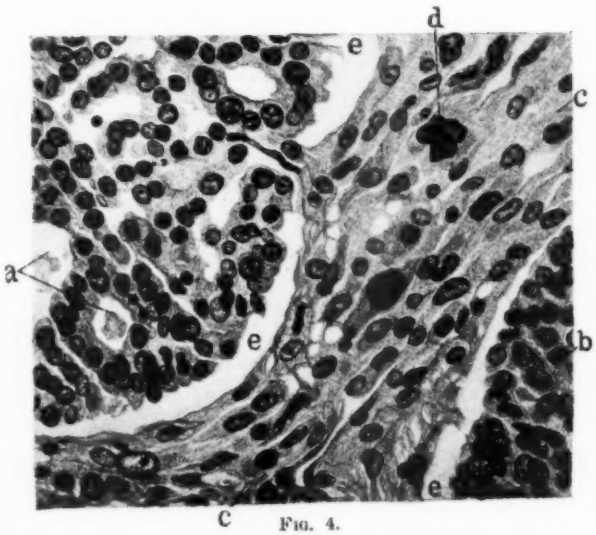

FIG. 4.

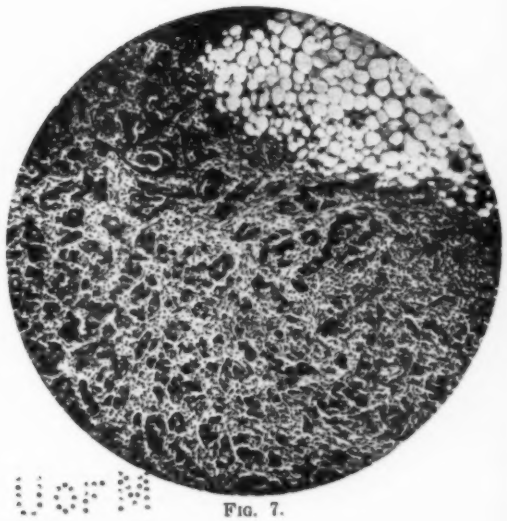

FIG. 7.

shaggy membrane. Small cystic spaces are scattered throughout the tumor. At *a* is seen the fine honey-combed appearance. At *c*, *d*, *e* and *g* the tissue is fairly homogeneous and looks like sarcoma. *f* is a small blood vessel.

FIG. 3.—Gyn. Path. No. 14414 (80 diameters). The two processes are well represented here. At *a* are seen the large gland lumina partially filled with coagulated fluid. The glands present the typical picture of adenocarcinoma. The stroma *c* shows a decidedly active and malignant picture. The majority of the cells are spindle shaped, but numerous large irregular cells, *d*, are found scattered throughout. The stroma is rich in blood vessels *e*.

FIG. 4.—Gyn. Path. No. 14414 (380 diameters). This illustration shows a magnification of the picture seen at Fig. 3, *b*. Note the large atypical cells lining the glands *a*. At *b* the glands are much less well defined. The stroma *c* consists of cells irregular in size, shape and staining qualities, and at *d* is shown a large so-called giant cell. Note the spaces *e* between the carcinomatous and sarcomatous processes, showing a tendency on the part of the carcinoma to retract from the sarcoma.

FIG. 5.—Gyn. Path. No. 15613. The section here pictured is taken from the recurrent tumor. The combined malignant processes are well marked. The sarcoma predominates and appears much more active than the process in the original tumor (Fig. 3).

FIG. 6.—Gyn. Path. No. 15613. This section shows a portion of the recurrent tumor which is purely sarcomatous in character. Note the number of large atypical cells.

FIG. 7.—Gyn. Path. No. 15613. This shows a section through the thickened and nodular omentum. The adenocarcinoma is well marked. The stroma shows no evidence of sarcoma.

THE BLOOD-PICTURE IN HODGKIN'S DISEASE.

By C. H. BUNTING, M. D.

(From the Pathological Laboratory of the University of Wisconsin.)

The blood-picture of Hodgkin's disease, as manifested in the various published cases, has been critically considered by Fabian[1] in a recent article, and his findings are summarized as follows:

(1) The most frequent blood-picture found in the course of Hodgkin's disease is a polymorphonuclear neutrophile leukocytosis of moderate grade.

(2) The blood-picture may be unmodified (about one-fifth of all cases).

(3) In about one-fifth of the reported cases there is a more or less well marked leukopenia, either present throughout the entire course, or transitory, and if the latter occurring more frequently in late stages.

(4) Qualitatively, the blood shows a relative neutrophile leukocytosis—that is, an increase in percentage up to 99 per cent and more; with a corresponding decrease in lymphocyte percentage to 3 per cent and, in two cases, to practically 0 per cent; most frequently at the same time with an absolute leukocytosis, at times with a leukopenia, and, rarely, with a normal count.

(5) In about one-fourth of the cases there was an eosinophilia, usually slight or moderate, seldom of marked degree.

(6) Very seldom one may find a mastzell increase.

(7) Scattered myelocytes were noted—very rarely enough to estimate.

(8) In one case an enormous increase in blood-platelets was noted.

(9) At times, though usually transitory, a slight, rarely a marked, lymphocytosis may be noted.

(10) In the course of the disease there develops a secondary anæmia, at first moderate, but later pronounced.

Fabian's general conclusions from his study of these cases is that while there may be characteristic features of the blood-picture in Hodgkin's disease, they are not constant enough to be of diagnostic value, and that in further study an attempt should be made to correlate the blood picture and that found in the glands. During the past three years the author has been making such a study in conjunction with Dr. J. L. Yates, of Milwaukee, and, while his findings are in general in agreement with those of Fabian, yet, on the other hand, they are sufficiently at variance to seem to warrant publication. There are two features of this study which may be emphasized, and which add to its value. In most of the cases at least one blood count has been made just previous to the removal of a gland for section, and further, all the smears have been examined by one person, the author, who has used the same staining and counting technique throughout.

In a previous paper[2] I have emphasized one of the most marked characteristics of the blood smears of Hodgkin's disease, that is, the presence of a large number of blood-platelets, inclusive of unusually large platelet forms, practically megalokaryocyte pseudopodia. This has been observed in all the eleven cases forming the basis of this report, both in early and in late cases, and over considerable periods of time in cases on which blood counts have been made at intervals.

From this constant finding and from pathological findings in autopsy material from cases of Hodgkin's disease, it was suggested in the previous report that the toxin of the disease acted as strongly upon the platelet-forming elements as upon the lymphocytes. An eventual necrosis of megalokaryocytes in the bone-marrow was found. One might have predicted from this finding that in late cases an exhaustion of platelets might take place, resulting in a low platelet count in the circulation. Such a case had not occurred in the author's series at the time of publication of his first report, but since then Case V of the series has shown such a change. After

[1] Wiener klin. Wchnschr., 1910, XXIII, 1515; Centralbl. f. allg. Path., 1911, XXII, 145.

[2] Johns Hopkins Hosp. Bull., 1911, 114.

having shown a high platelet content of his blood in counts at intervals from November 9, 1909, to September, 1910, the boy returned to the Columbia Hospital, Milwaukee, in April, 1911 with serious hæmorrhages from the mucous membranes, with a secondary anæmia, a leukopenia—3500 to 4000—and fewer platelets than leukocytes, as shown by repeated examinations made during April and May. However, while exceptional or terminal cases may show this platelet exhaustion, the excessive number would appear to be constant in the course of the disease.

Coincident with this platelet study, careful study of the leukocyte picture in the disease has been made and has led to the conclusion that in the combined platelet and leukocyte picture one has features that are very characteristic and, in fact, almost pathognomonic of Hodgkin's disease. While from my experience I believe that the diagnosis may be made from examination of the blood smear, I would not recommend the method to the exclusion of the histological examination of an excised gland. The latter method is too simple to neglect, but, where glands are inaccessible, or where permission for removal is not obtained, the examination of blood smears is very helpful, and is especially convincing if backed by a negative von Pirquet reaction.

In this study, blood smears from eleven cases of Hodgkin's disease have been carefully examined and differential counts made. In a few cases several counts have been made at intervals of some months, giving confirmatory evidence of the value of the picture. The cases have varied in their stage of development from early cases to those a few months from the fatal termination, so that it has been possible to note the changes which take place in the blood-picture with the development of the disease.

The blood smears have been stained with Wright's stain for the purposes of the counts, although Ehrlich's triple stain has been used for the determination of certain features. Five hundred cells have been the routine and the smallest number counted, but in some cases this has been exceeded. The leukocytes have been grouped into seven classes, except in a few of the early counts where but six were made. These groups are: (1) Polymorphonuclear neutrophile (N.); (2) Eosinophile (E.); (3) Basophile (mastzell) (B.); (4) Small lymphocyte (S. L.); (5) Large lymphocyte (L. L.); (6) Large mononuclear (L. M.); (7) Transitional (Tr.).

While the first three groups need no explanation, a word may be due as to the divisions of the so-called mononuclear or non-granular groups. Study of blood smears from normal individuals, stained with the Romanowsky stains, shows four distinct types of mononuclear cells. However, in studying large numbers of these cells, one finds that the distinctions in size and staining reaction are not always sharply made; that is, the groups overlap somewhat, so that the separation becomes more or less arbitrary. This is especially the case in regard to the small and large lymphocyte groups, and in regard to the large lymphocyte and the large mononuclear. In the earlier counts the last two groups were included under a single head. Although this grouping may be artificial and arbitrary, the same standards were employed throughout in forming a judgment, and the separation may be of some value.

The groups are characterized as follows:

(1) *Small Lymphocyte.*—A cell with deeply staining nucleus, which scarcely exceeds a red-blood cell in diameter, and with a scant rim of basophilic protoplasm.

(2) *Large Lymphocyte.*—A cell usually almost the size of a neutrophile leukocyte with nucleus larger than that of the preceding class, and with protoplasm more abundant, less basophilic as a rule, and containing numerous coarse, oftentimes almost rod-like metachromatic granules.

(3) *Large Mononuclear.*—A cell larger than a neutrophile leukocyte, with large round or oval nucleus and considerable protoplasm, staining a fairly deep blue and containing at times a few fine metachromatic granules.

(4) *Transitionals.*—The largest cells of the groups, with nuclei of various shapes, from simple indented nuclei, to lobed, mulberry-shaped, or even ring-shaped nuclei; and with abundant clear, light-blue protoplasm thickly dotted with fine metachromatic granules which do not stain with Ehrlich's triple stain.

As the transitional leukocyte forms a prominent feature of the differential picture in Hodgkin's disease, a further word in regard to it seems necessary. It is quite evidently misnamed, for it bears no relation to the polymorphonuclear neutrophile. To one "brought up" medically on the Ehrlich stain, this cell as revealed by Wright's stain comes as a surprise. With the Ehrlich stain, the nucleus is but faintly stained and its structure is poorly brought out, while the protoplasm usually appears as an unstained halo, or with but a slight tint and with but an occasional granule. With Wright's stain, however, the nucleus stains sharply. It is massive and of a protean variety of shapes—knobbed, lobed, twisted, folded, ring-shaped. So complex are the nuclei, at least in Hodgkin's smears, that one is at first inclined to believe he is dealing with a foreign cell. Yet the cell is present in normal smears to the extent of from 6 to 8 per cent of the leukocyte count, and the nuclei appear almost if not fully as complex as in Hodgkin's smears. The protoplasm of the cell stains a clear blue and is crowded with fine azure granules finer than those of the neutrophile leukocyte. They are finer also than the platelet granules, but have the same tint. As noted above, they are unstained by the Ehrlich stain. I do not desire to discuss the relation of the transitional cell to other cells or to enter into the question of its origin, further than to say that cells morphologically and tinctorially similar may be found in smears from normal lymph glands.

Preliminary to the detailing of the blood counts in the Hodgkin's cases examined, it should be said that all of the smears, with the exception of the late ones in Case V, showed very abundant platelets and in every case also large platelet forms and pseudopodia were present. The leukocyte examinations and the brief clinical points necessary, follow:

CASE I (Dr. Yates).—November 20, 1908. Male, white, 21. Onset of disease, July, 1908. Cervical and axillary glands involved. Test gland removed October 30, 1908, showed early Hodgkin's changes. Gradual improvement under treatment. Blood counts:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.		L. M.	Tr.
XI. 20, '08.....	5,301,000	7,500	51.2	3.2	1.6	25.4		10.		8.6
III. 4, '09....	4,968,000	4,800	55.2	2.4	0.8	23.6		6.6		11.4
VI. 11, '09.....	5,000,000	7,000	65.8	2.8	0.0	16.8	7.6		1.2	5.8
II. 16, '10.....	5 800,000	7,000	59.8	4.0	1.4	15.4	8.8		1.8	8.8
VI. 9, '11.....	.....	8,500	65.0	2.6	1.2	21.2	3.		0.6	6.4

CASE II (Dr. Yates).—Male, white, 10. Large mass of discrete glands in left cervical region of at least one year's duration previous to removal, November 10, 1908. Glands show well-marked Hodgkin's picture. Von Pirquet reaction negative October 8, 1910. Gradual improvement under treatment. Blood counts:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.		L. M.	Tr.
IV. 1, '09.....	4,712,000	9,500	56.2	8.6	0.4	16.4		7.4		11.0
I. 22, '10.....	5,250,000	9,600	63.6	3.6	0.0	12.0	12.0		2.0	6.8
III. 12, '10.	.....	.....	53.4	5.2	1.0	13.	16.		1.6	9.8
X. 8, '10.....	4 980,000	9,800	53.2	5.2	0.4	27.8	4.		1.4	8.

CASE III.—April 1, 1909. Male, white, 30. Seen 2 weeks after second operation for glands of neck. First operation 6 months previous at Rochester. Diagnosis, Hodgkin's disease. Blood counts:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.		L. M.	Tr.
IV. 1, '09.....	4,560,000	10.000	79.4	0.2	0.4	5.8		3.4		10.8

CASE IV (Dr. Tupper, Eau Claire, Wis.).—February 5, 1910. Female, white, 40. Onset, — months previous in right inguinal glands. Subsequent involvement of left inguinal, left axillary, left and right cervical glands. Test gland shows well-marked active Hodgkin's picture. Death in October, 1910. Blood count:

Date.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
II. 5, '10.....	36.	0.6	0.2	39.2	10.6	2.8	10.6

CASE V (Dr. Yates).—November 9, 1909. Male, white, 8 years. Enlargement of cervical glands began 5 months previous to date. Left inguinal glands also enlarged. Test gland, November 30, 1909, shows hyperplastic stage of lesion. January, 1910, cervical glands removed. October, 1910, von Pirquet test negative. April, 1911, mucous membrane hæmorrhages, anæmia. Blood counts:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.		L. M.	Tr.
XI. 9, '09.....	.....	9,900	59.4	4.6	0.4	21.8		3.6		10.2
XI. 30, '09.....	.....	.....	50.8	5.8	0.6	26.8		7.2		8.8
II. 26, '10.....	5,000,000	5,000	55.2	1.4	0.4	22.4	9.2		2.0	9.4
IX. 7, '10.....	5,160,000	8,700	59.4	1.	1.2	16.4	6.6		6.	10.4
IV. 21, '11.....	3,456,000	4,800	63.2	1.8	1.	10.2	4.6		1.4	17.8
Transfused.										
IV. 24, '11.....	3,176,000	3,800	54.	6.8	0.2	17.8	4.8		1.8	14.6
V. 2, '22.....	2,624 000	8,700	67.6	1.4	1.4	6.8	9.6		0.6	12.6
Transfused.										
V. 5, '11.....	2,760,000	4,500	54.6	2.6	2.	18.8	7.6		0.6	13.8
V. 9, '11.....	3,200,000	4,000	50.8	4.	1.6	25.8	6.4		0.6	10.8
Transfused.										
V. 10, '11.....	.....	..	00.	9.8	0.6	8.2	6.8		0.4	14.2
V. 13 '11.	3,400.000	3,500	56.2	4.8	0.8	17.6	6.4		0.4	13.8
V. 22, '11.....	3,712,000	3,400	55.8	3.2	0.0	19.8	3.6		1.2	16.4
V. 29, '11.... ..	3,680,000	3,600	56.4	3.4	1.6	18.	8.1		0.6	11.8

CASE VI (Dr. Sullivan, Madison, Wis.).—March 1, 1910. Male, white, 16. Left cervical glands much enlarged. Marked induration of neck. Enlargement noted for only 1 month, but the amount of sclerosis in test gland suggests greater duration. March 10, wound resulting from removal of gland for diagnosis still unhealed. May 13, wound healed but induration of neck marked. Blood counts:

Date.	W.b.c.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
III. 10, '10.....	18,000	81.6	0.6	0.4	4.2	3.	1.6	8.6
V. 13, '10.....	27,000	80.6	1.6	0.0	7.8	2.8	0.8	6.4

CASE VII (Dr. Bennett, Oregon, Wis.).—January 5, 1910. Female, white, 64. In October, 1909, general glandular enlargement with clinical diagnosis of Hodgkin's disease. Death June 30, 1910. Blood count:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
X. 24, '09.....	3,200,000	4,480							
I. 5, '10.....	.....	.....	51.8	4.2	0.4	20.0	9.8	1.6	9.2

CASE VIII (Dr. Yates).—Male, white, 33. Onset in March, 1907, with supraclavicular glandular enlargement. In September, 1908, supraclavicular and left axillary glands most enlarged. Some enlargement of right cervical, axillary and inguinal glands. October 30, 1908, excised gland shows typical and advanced Hodgkin's disease. Death occurred May 20, 1909. Blood count:

Date.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
I. 10, '09.	76.2	1.4	0.6	7.6	6.0		8.2

CASE IX (Dr. Yates).—October 3, 1910. Male, white, 5. Marked enlargement of left cervical glands of 5 months duration. Test gland shows well-marked Hodgkin's changes. Death from shock at operation. Blood count:

Date.	R. b. c.	W.b.c.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
X. 3, '10.....	5,160 000	4,200	54.4	2.4	0.2	22.6	6.6	2.4	9.4

CASE X (Dr. Yates).—Male, white, cervical Hodgkin's. Count made 2 months previous to death of patient.

Date.	W.b.c.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
IV. 30, '10.....	14,300	84.	0.0	0.0	3.8	1.0	1.0	10.2

CASE XI (Dr. Baird, Eau Claire, Wis.).—December 8, 1910. Male, white, 22. Enlargement of supraclavicular gland noted one year previous. Axillary glands enlarged at date. Test gland shows definite Hodgkin's picture. Blood count:

Date.	N.	E.	B.	S. L.	L. L.	L. M.	Tr.
XII. 8, '10.....	81.8	0.2	0.6	2.6	2.6	1.	11.2

When one examines these counts critically in an attempt to correlate the counts with definite stages of the disease process, he is confronted with difficulties arising from the facts that all parts of the lymphoid tissue are not affected, and further, that, of any large group of glands affected by the disease, the individual glands may show different stages of development of the process. Yet there are some points in the counts which stand out definitely. The most striking feature perhaps is the constant high percentage of the so-called transitional cells. This high percentage occurs not only when the total leukocyte count is approximately normal, but also is maintained even when there is a sharp leukocytosis. With a normal total count of leukocytes the percentage of transitionals approximates 10; with a very marked leukocytosis, as in Case VI (27,000), one may have a reduction (6.4 per cent); while in a leukopenia, as in Case V, the percentage rises to 17.8 in a total of 4800. The series indicates, then, that throughout the disease there is a relatively large number of these cells in the circulation. When one recalls that similar cells are found in smears from normal lymph glands, and also that in Hodgkin's disease there is a marked proliferation of the endothelial elements of the glands, it is difficult not to draw the conclusion that such a proliferation results in this excessive transitional content of the blood. Such a suggestion, however, cannot be considered as proved.

The lymphocyte count has varied much in these cases, but there is a definite tendency for a percentage decrease from a normal or slightly increased count in early and active stages to a very low count in later stages. Thus in Case IV we find

49.8 per cent of small and large lymphocytes in an active phase; in Case V, 31.6 per cent; in Case IX, 31.2 per cent. On the other hand, in the advanced cases, X, XI, III, we find from 4 to 8 per cent.

With this decrease in lymphocyte percentage, we find a corresponding increase in the polymorphonuclear count, from a relatively normal count during the course of the disease, to a relatively high count (76.2, 79.4, 81.8, 84 per cent) in the terminal stages or when the periglandular infiltration and induration are marked. The neutrophiles appear therefore to be unaffected except by extra-glandular processes and not by the changes taking place within the glands themselves.

Quite the opposite is the relation of the disease to the eosinophile. Eosinophiles are found in the glands in large numbers. Remembering that the count of cells in the peripheral blood represents but the ratio of supply to demand, it is not surprising to find very low counts of eosinophiles during the active progress of the disease (0.6 per cent or less in six of the cases). In reactive or quiescent cases, however, the count is higher, either toward the upper limit of normal, or slightly above. The highest count found was 8.6 per cent in Case II, if one excepts the 9.8 per cent found in Case V twenty-four hours after transfusion. If, as seems probable to the author, from a study of lymph glands at autopsy in a variety of conditions, the products of destruction of lymphocytes are positively chemotactic for eosinophiles, and if the findings above are not exceptional, the eosinophile count in cases of Hodgkin's disease would seem a good index of the progress or activity of the disease.

There is no striking change in the basophile count, or in that of the large mononuclears.

While these deviations of the Hodgkin's blood-picture from the normal are pronounced, the question naturally arises as to how they compare with counts in other diseases of the lymph glands. My series of counts in other conditions is not large, but in none of the conditions have I found the combined platelet-leukocyte picture that has been found in Hodgkin's disease.

In tuberculosis of the gland the platelet count is high, but in smears from four cases I have not found the large forms which are common in Hodgkin's. The transitional leukocytes are on the upper limit of normal or slightly above. The four differential counts are as follows:

	W.b.c.	N.	E.	B.	S. L.	L. L.	L.M.	Tr.
1	9,000	41.6	2.4	0.0	43.2	4.4	0.4	8.
2	.....	56.	1.8	0.2	26.4	5.	3.	7.6
3	.....	63.	1.2	0.6	19.	6.	2.2	8.
4	.....	64.8	1.8	0.2	19.4	6.	1.	6.4

In two cases of relatively acute non-specific lymphadenitis following throat infections, the following differentials were obtained:

	N.	E.	B.	S. L.	L. L.	L.M.	Tr.
1	72.2	0.2	0.2	14.6	2.2	1.8	8.8
2	47.8	4.	0.6	30.6	5.4	1.6	10.8

In these one finds quite the picture seen in active and early stages of Hodgkin's disease as far as the leukocytes are concerned. This is what one might expect, if the analysis of the Hodgkin's picture given above is correct. In both of these cases the striking platelet-picture of Hodgkin's disease was lacking.

Finally, in one case of chronic simple sclerosis of the lymph glands of obscure origin, there was obtained the following count, with a low number of blood-platelets:

N.	E.	B.	S. L.	L. L.	L.M.	Tr.
72.	10.0	0.8	11.8	1.4	0.4	5.6

These counts are too few to establish a blood-picture for the various conditions, yet they do not vitiate the general conclusions of the author from his study of Hodgkin's disease, that the blood-picture is characteristic, is indicative of what is transpiring in the glands, and may be, if carefully weighed, a help in diagnosis.

THE TRANSPLANTATION OF FREE FLAPS OF FASCIA.

AN EXPERIMENTAL STUDY.

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Introduction.—For some time I have been interested in the methods brought forward for replacing and for reenforcing weakened or defective tissues, and while some of the methods are admirable, all are limited in their application. It seemed worth while to search for a material which would accomplish the same purpose but would have a wider field of usefulness.

In looking about for some suitable tissue in the body which was easily obtainable, which had considerable strength, and at the same time was sufficiently flexible for any desired need, I was led to try the experimental transplantation of free flaps of fascia.

After proceeding with the experiments for sometime I found that some excellent work had already been done along this line.[1] However, my results were sufficiently suggestive to warrant a report on the subject, in order to again call attention to this promising surgical procedure.

[1] Kirschner, M.: Ueber freie Sehnen- und Fascien Transplantation. Beitr. z. klin. Chir., 1909, LXV, 472.

Günther: Ueber Duraplastic: eine klinisch-experimentelle Studie. Beitr. z. klin. Chir., 1910, LXIX, 740.

Hohmeier: Ueber ein neues Verfahren zur Deckung von Trachealdefekten. München. med. Wchnschr., 1911, LVIII, 948.

Since this paper was handed in for publication the following

Sixty-two experiments were done on thirty-nine dogs. Ether anesthesia was used in each experiment.

Technic.—The part was shaved, washed with green soap and water, then with alcohol and ether. After the skin was thoroughly dry it was painted with tincture of iodin, 2.5 per cent. The iodin solution was also freely used in the open wounds and after suture of the skin.

Fine black silk was the ligature and suture material used throughout. The wounds were closed in layers wherever possible. The skin was closed in every instance with the buttonhole stitch.

Dry sterile gauze secured by a bandage was used wherever dressings were applied.

The fascia was obtained, for the most part, from the thigh, the ilio-tibial band of the fascia lata being the most satisfactory portion to work with, as it is easily separated from the underlying tissues. In a few instances the strong abdominal fascia was employed.

The fascia was transplanted in both single and double layers and in one or two instances was twisted.

In each experiment where adhesions were not desired the fascia lata (ilio-tibial band) was placed with the inner or muscle surface exposed. For example, when a flap of fascia was placed in a peritoneal defect, the muscle or smooth side was turned toward the peritoneal cavity, and it was found that dense adhesions were less likely to occur than when the outer side was turned towards the cavity.

In this series, unless otherwise stated, the fascia was transplanted into the same animal from which it was taken.

An attempt was made to place free flaps of fascia on the various tissues, in order to test its vitality and obtain an idea of its possibilities for clinical use.

Experiments.—For convenience I have divided the series into eight groups. To economize space I will only report a few of the typical experiments in each group.

GROUP I.—TRANSPLANTATION OF FREE FASCIA INTO SUBCUTANEOUS TISSUE ON FAT, MUSCLE, PERIOSTEUM, NAKED BONE, CARTILAGE, TENDONS AND LIGAMENTS.

EXPERIMENT 6.—Male, black mongrel; about 9 months old.

Operation.—November 22, 1910. A piece of fascia lata was sutured in the subcutaneous tissue of the chest wall. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

February 23. Distemper. The animal was sacrificed. *Autopsy.*—The fascia was somewhat thickened but otherwise it seemed normal. It was strong and tough.

Histology.[2]—(Microscopic examination.) Showed apparently normal fascia with fibers and nuclei clearly stained. No degeneration.

EXPERIMENT 7.—Female, white fox terrier; about 6 months old.

Operation.—November 28, 1910. The sartorius muscle was exposed and a broad band of fascia lata was sutured snugly around it. The wound was closed in the usual manner. No dressing. Condition on leaving the table excellent. *Per primam* healing.

January 16, 1911. Animal sacrificed. *Autopsy.*—The fascia was somewhat thickened but otherwise it seemed normal. The fascia band could be easily stripped from the muscle.

Histology.—(Microscopic examination.) The sections showed normal fascia with no signs of degeneration.

EXPERIMENT 8.—Female, tan mongrel; about 6 months old. November 29, 1910. A flap of fascia lata was removed from the thigh and wrapped in moist salt gauze and then placed in the ice box in a sterile jar.

Operation.—December 1, 1910. The fascia which was placed in the ice box 48 hours before was sutured on the ribs, under the muscle. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

January 24, 1911. Animal sacrificed. *Autopsy.*—The fascia was thickened but otherwise it seemed normal. It was movable on the ribs.

Histology.—(Microscopic examination.) The sections showed normal fascia with clearly stained nuclei and fibers.

EXPERIMENT 9.—Male, black and white fox terrier; about 2 years old.

Operation.—December 1, 1910. The right femur was exposed and the periosteum was stripped back for about 2 cm. Into this defect a band of fascia lata was sutured around the bone. The wound was closed in the usual manner. No dressing. Condition on leaving the table excellent. *Per primam* healing.

December 27. Death from pneumonia. *Autopsy.*—The band of fascia was somewhat thickened and was intimately blended with the periosteum on either side. The structure of the fascia could be plainly seen.

Histology.—(Microscopic examination.) The sections showed normal fascia with no signs of degeneration.

EXPERIMENT 43.—Female, white mongrel; about 2 years old.

Operation.—March 14, 1911. The trachea was exposed and a large flap of fascia was sutured on it. This fascia had been removed from another animal on February 7, 1911, and had been in cold storage since that date. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

April 10. Death from distemper. *Autopsy.*—The fascia was somewhat thickened but otherwise it seemed normal. It was closely adherent along the margins and seemed to blend with the tissues on the surface of the trachea.

Histology.—(Microscopic examination.) The sections showed normal, well-nourished fascia.

Comment.—In this group free fascia flaps were successfully transplanted into the subcutaneous tissue, into fat, on muscle, periosteum, bone, cartilage, tendons and ligaments.

Microscopic examination of the specimens showed that the fascia retained it own structure after transplantation and was apparently healthy and well nourished. This was true

experimental-clinical articles have appeared. They will be considered fully in another report.

Hohmeier, F.: Experimente über Verschluss von Wunden und Ueberbrückung von Defecten Schleimhauttragender Körpercanäle und -höhlen durch freie auto-plastic. Arch. f. klin. Chir., 1911, p. 345.

König, F.: Neue Wege der plastischen Chirurgie. (Verschluss und Ueberbrückung.) Arch. f. klin. Chir., 1911, XCIV, 326.

Lewis, D. & Davis, C. B.: Experimental Direct Transplantation of Tendon and Fascia. J. Amer. Med. Assoc., 1911, LVII, 540.

[2] I take this opportunity of thanking Dr. C. D. Deming for assistance in the histological examinations.

even after the fascia had been kept in cold storage for thirty-five days and then transplanted into another animal.

The clinical uses suggested by these experiments are of considerable importance, and cover a wide field.

GROUP II.—TRANSPLANTATION OF FREE FASCIA INTO TENDON AND MUSCLE DEFECTS.

EXPERIMENT 16.—Male, black mongrel; about 6 months old.

Operation.—December 19, 1910. The right tendo Achillis was exposed and a section about 2.5 cm. long was removed. The stumps were held in position by a strong tension suture, and then a flap of fascia lata was placed in the defect so as to surround the stumps like a tube. This tube was then drawn tight and the ends were securely sutured around the stumps. The tension suture was cut and the dead spaces obliterated. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

FIG. 1.—*Experiment 16.* Fascia to replace tendo Achillis. Operation, December 19, 1910. Specimen removed, March 7, 1911. Comparison of new and normal tendons. The new tendon is thicker than the normal. The + marks the operated leg.

March 7, 1911. Distemper. Sacrificed. The animal had been very active and had no limp. It was imposible to tell which leg had been operated on without close inspection. *Autopsy.*—The replaced tendon was thicker than normal, but seemed strong and satisfactory in every way. (Fig. 1.)

Histology.—(Microscopic examination.) Cross section of the new tendo Achillis showed normal staining fascia which was folded on itself. Surrounding the fascia was connective tissue, which caused the apparent thickening of the new tendon.

EXPERIMENT 20.—Male, white fox terrier; about 4 months old.

Operation.—January 3, 1911. The sartorius muscle was exposed and a section about 2.5 cm. long was removed. The muscle ends were held in position and a flap of fascia lata was sutured into the defect surrounding the muscle stumps by a tube of fascia. The dead space was obliterated and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

February 1. Death from pneumonia. Since the healing the animal had been very active and no difference could be detected in the gait. *Autopsy.*—The fascia was firmly united with the muscle ends. (Fig. 2.)

Histology.—(Microscopic examination.) The sections showed fascia with fibers and nuclei clearly stained.

Comment.—This group shows that muscle and tendon defects may be bridged by free flaps of fascia. Muscle defects may be bridged by means of fascia flaps and thus a certain amount of the muscle function saved. The fascia united firmly with the muscle ends and formed a strong symmetrical band between them.

FIG. 2.—*Experiment 18.* Fascia replacing defect in sartorius muscle. Operation, December 27, 1910. Specimen removed, January 14, 1911. The thick muscle ends can be seen, and connecting them is the fascia which has united firmly to them.

The use of fascia flaps to replace tendons is of especial importance and most promising clinically. While it is a well-known fact that free tendon transplantation can be successfully done, it must be borne in mind that it is often difficult to secure either long or short pieces of tendon without doing considerable damage.

There are large amounts of fascia available in the body which can be secured without damage to any other working part. Thus tendons of any desired length might be made from strips of the ilio-tibial band of the fascia lata.

Experimentally the tendons made of folded strips of fascia are not liable to adhere to surrounding tissues. Fascia flaps might also be used to prevent tendons from being caught in scar tissue. The final results after replacing tendons with this material are more satisfactory than with any foreign material or transplantable tissue with which I am familiar.

GROUP III.—TRANSPLANTATION OF FREE FASCIA AROUND VESSELS AND NERVES.

EXPERIMENT 33.—Female, black and yellow mongrel; about 1 year old.

Operation.—February 14, 1911. The right jugular vein was dissected out and a flap of fascia lata was wrapped about it. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

March 3. Death from pneumonia. *Autopsy.*—The fascia was thickened but otherwise seemed normal. It was quite adherent to the vessel wall. The lumen of the vessel was not encroached upon.

FIG. 3.—*Experiment 41.* Fascia around vessels and on trachea. Operation, March 14, 1911. Specimen removed, April 11, 1911. On the right carotid can be seen a flap of fascia which was transplanted immediately from the same animal. On the left carotid and trachea are flaps of fascia from another animal which had been in cold storage for 35 days.

Histology.—(Microscopic examination.) The sections showed the structure of the vessel to be normal. It was surrounded by a band of fascia which was apparently well nourished and showed no signs of degeneration.

EXPERIMENT 41.—Female, yellow and white mongrel; about 1 year old.

Operation.—March 14, 1911. Both common carotid arteries were exposed. Around the right carotid a piece of fascia lata was sutured, which had just been removed from the right thigh. Around the left carotid was sutured a piece of fascia which had been removed from another animal on February 7, 1911, and had been in cold storage since that date. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

April 10. Death from pneumonia. *Autopsy.*—The fascia on both carotids was thickened, but otherwise seemed normal. The appearance of the two specimens was the same. The fascia was quite adherent to the vessels but could be stripped off. The lumen of the vessels was not encroached upon. (Fig. 3.)

Histology.—(Microscopic examination.) The sections showed apparently normal fascia in both instances. No signs of degeneration.

EXPERIMENT 44.—Male, black and white fox terrier; about 1 year old.

Operation.—March 21, 1911. The right sciatic nerve was exposed and a flap of fascia lata was sutured around it. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing. Gait unaffected.

April 20. Distemper, animal sacrificed. *Autopsy.*—The fascia was thickened but otherwise seemed normal. It could be moved on the nerve to a slight degree. There was no constriction of the caliber of the nerve.

Histology.—(Microscopic examination.) The sections showed a normal nerve surrounded by well-nourished, apparently normal, fascia.

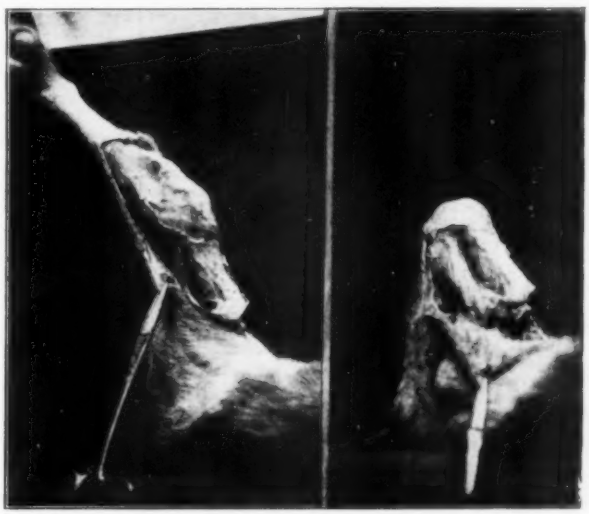


FIG. 4.—*Experiment 22.* Fascia filling defect made by removal of patella. Operation, January 9, 1911. Specimen removed, February 2, 1911. Note the amount of extension and flexion possible. The fascia can be seen firmly healed to the joint capsule.

Comment.—This group shows that free flaps of fascia may be successfully transplanted around arteries, veins and nerves, without in any way interfering with the lumen of the vessels, or compressing the nerves.

Clinically, fascia flaps might be of use in protecting suture lines in vessel surgery and in reenforcing weakened areas in vessel walls. The site of nerve plastic operations might be surrounded and protected by such flaps. It might also be of use in protecting a nerve after it was freed from callus or scar tissue.

GROUP IV.—TRANSPLANTATION OF FREE FASCIA INTO JOINTS AND FOR SUTURING FRACTURED BONES.

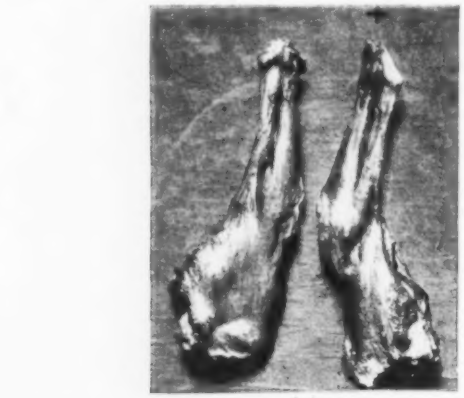
EXPERIMENT 22.—Female, yellow mongrel; about 6 months old.

Operation.—January 9, 1911. The left patella was removed and a piece of fascia lata was substituted for it. The fascia

was folded on itself so that its inner smooth surface was next to the joint, and also under the skin. It was sutured to the capsule and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

February 2. Pneumonia, animal sacrificed. The joint was freely movable and as far as could be seen had been as serviceable as the normal knee. (Fig. 4.) *Autopsy.*—The fascia was easily separated from the skin. It had adhered firmly to the joint capsule. On opening the joint the surface of the fascia was perfectly smooth. There were no adhesions. The fascia was slightly thickened.

Histology.—(Microscopic examination.) The sections showed a double thickness of apparently normal fascia. The staining of fibers and nuclei was well marked. (Fig. 5.)



(a)

(b)

(c)

FIG. 6.—*Experiment 29.* Fascia into joint after removal of the cartilage. Operation, February 6, 1911. Specimen removed, February 28, 1911. (a) Leg extended, compared with normal. (b) Leg flexed, compared with normal. (c) Inside of joint. The + marks the operated joint.

EXPERIMENT 29.—Female, white fox terrier; about 8 months old.

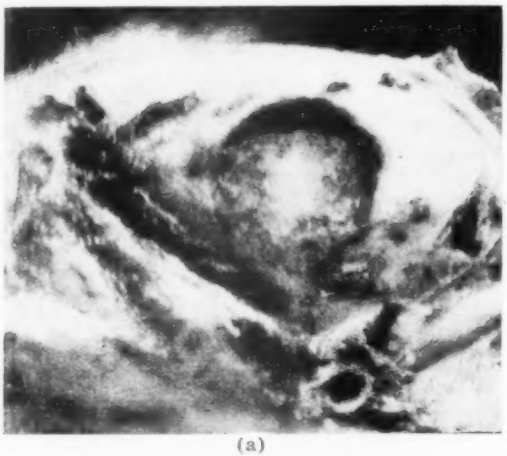
Operation.—February 6, 1911. The right knee-joint was opened and the entire articular cartilage was removed as thoroughly as possible. Then a piece of fascia lata was inserted and sutured over the denuded portion of the femur and well up under the patella. The joint was closed. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

February 27. Death from pneumonia. Since the dressing was removed the animal has been using the operated knee-joint without apparent discomfort. *Autopsy.*—The joint was movable. The fascia was slightly thickened. It was adherent to the denuded end of the femur, but to no other portion of the joint. Its structure was well preserved. (Fig. 6.)

Histology.—(Microscopic examination.) The sections showed normal staining, well-nourished fascia. No signs of degeneration or absorption.

EXPERIMENT 31.—Male, yellow and white mongrel; about 6 months old.

Operation.—February 13, 1911. The right tibia was exposed and the periosteum stripped back. The bone was sawed through and then two strips of fascia lata were passed through drill holes and tied. The tied ends were made additionally secure by sutures. The wound was closed and a small drain was inserted in the lower angle. Dry dressing, crinolin and splint.



(a)

(b)

FIG. 7.—*Experiment 38.* Fascia into skull and dura defect. Operation, March 6, 1911. Specimen removed, April 20, 1911. (a) Bone defect from outside with fascia adherent to bone edges. (b) From within the outline of the bone defect can be seen. The fascia is closely adherent to the dura which extends beyond it. The fascia is smooth except for one small adhesion in the center.

Condition on leaving the table excellent. The stitches were removed on the fifth day. The wound was apparently nicely healed. It was practically impossible to immobilize the broken bone.

February 23. Distemper, animal sacrificed. *Autopsy.*—On removing the dressing the wound was found badly infected. In spite of the infection the strength of the fascia was apparently but little affected and the strips were still holding the ends of the bone together. This specimen was accidentally lost.

Comment.—This group is also interesting. Free flaps of fascia were successfully transplanted into joints and also to take the place of patellæ which had been removed. Both of these procedures are suggestive clinically.

Bones were fractured and the fragments sutured with strips of fascia. The result of these last experiments were unsatisfactory on account of the difficulty in immobilizing the fragments. However, the use of fascia strips in the open treatment of fractures in human beings may be of great use clinically, as immobilization can be secured.

The fascia does not act as a foreign body and has strength enough to stand any reasonable strain put upon it.

GROUP V.—TRANSPLANTATION OF FREE FASCIA INTO DEFECTS IN THE SKULL AND DURA, ALSO INTO TRACHEAL DEFECTS.

EXPERIMENT 38.—Male, yellow mongrel; about 1 year old.

Operation.—March 6, 1911. The left temporal muscle with the underlying periosteum was turned back and a ¾-inch button of bone was removed. The dura under this area was excised and a flap of fascia lata was tucked under the bone edges. The smooth muscle side of the fascia was placed next to the brain. The temporal muscle was replaced and sutured, and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

April 20. Distemper, animal sacrificed. *Autopsy.*—There was one small adhesion of the cortex to the central portion of the fascia. The edges of the fascia and dura were intimately blended. The structure of the fascia could be plainly seen. The fascia was tightly stretched across the bone defect and was firm and did not bulge on pressure. (Fig. 7.)

Histology.—(Microscopic examination.) The sections showed normal staining, apparently well-nourished fascia.

EXPERIMENT 62.—Female, black mongrel; about 1 year old.

Operation.—June 12, 1911. The trachea was exposed and an area 8 mm. square was excised. Over this defect was sutured securely a flap of fascia lata. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing. There was no cough or any respiratory symptom following the operation.

July 3. Animal sacrificed. *Autopsy.*—The fascia was somewhat thickened and firmly adherent to the surface of the trachea. There had been no leakage whatever. On opening the trachea from behind, the defect was made out as a very shallow depression and the fascia seemed to be entirely covered with mucous membrane, which had grown over it. (Fig. 8.)

Histology.—(Microscopic examination.) The sections showed the defect filled by normal staining, apparently well-nourished fascia. Over this fascia, as a base, the mucous membrane had grown, completely covering it. (Fig. 9.)

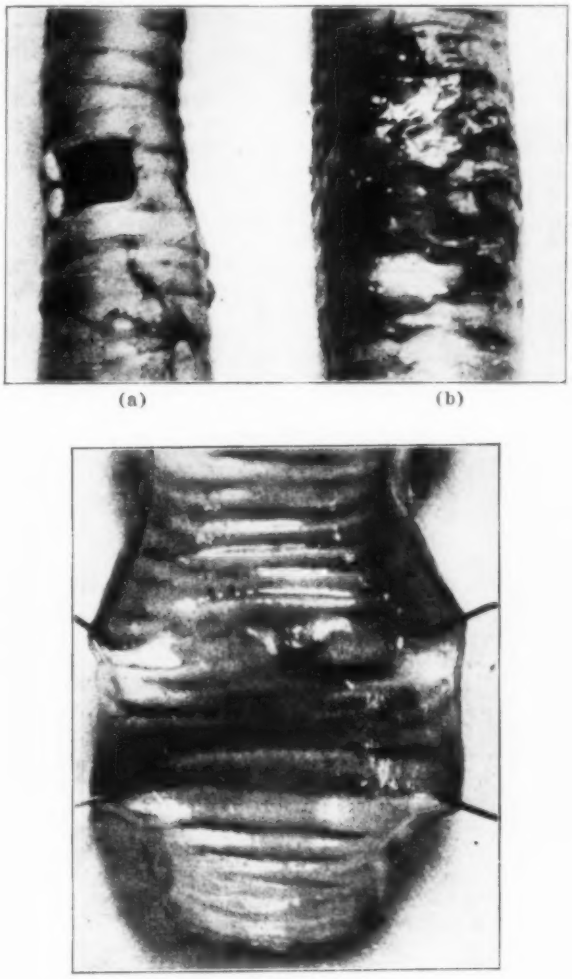
Comment.—This group shows that flaps of fascia inserted in skull defects between the dura and bone edges will heal and give a strong membrane which will resist considerable pressure from within and without. When the dura is removed in addition to the bone the fascia flap tucked under the bone edges will unite with the dura and also become tightly adherent to the bone edges.

There was in each instance a single fine adhesion of the cortex to the center of the fascia flap.

Fascia flaps might be used clinically in repairing skull defects and as an aid in the closing of a spina bifida.

This group also shows that free flaps of fascia may be successfully used to cover prepared defects in the trachea, without subsequent infection, and that the mucous membrane grows across the fascia covering the defect.

It might be of use, clinically, in closing old tracheotomy wounds, where there has been considerable destruction of cartilage, and also in reenforcing sutures of the trachea.



(a) (b) (c)

FIG. 8.—*Experiment 62.* Fascia over defect in trachea. Operation, June 12, 1911. Specimen removed, July 3, 1911. (a) Shows normal trachea with opening in it the size of that covered by the fascia. (b) The fascia healed over a similar defect. (c) The same specimen from within, showing a slight depression which marks the defect. The mucous membrane has grown completely over the fascia.

GROUP VI.—TRANSPLANTATION OF FREE FASCIA INTO PREPARED DEFECTS IN THE ABDOMINAL WALL.

EXPERIMENT 17.—Male, white and black fox terrier; about 1 year old.

Operation.—December 22, 1910. All the tissues of the abdominal wall between the skin and the peritoneum were excised from an area about 4 x 7 cm. Into this defect a flap of fascia

lata 3 x 6 cm. was sutured. The skin was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

June 27, 1911. Animal sacrificed. *Autopsy.*—There was no hernia or bulging of the abdominal wall at the site of operation. From within there was no depression in the parietal peritoneum. On holding the specimen to the light the outline of the inserted fascia could be readily seen. The fascia itself was slightly thickened but normal in every way and was strong and tough.

Histology.—(Microscopic examination.) The sections showed normal staining fascia with no signs of degeneration.

Experiment 19.—Male, brown and black mongrel; about 1 year old.

Operation.—December 29, 1910. The peritoneum was exposed and an area 4 x 2 cm. was excised. Into this defect a piece of fascia lata was sutured. The wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

February 7, 1911. Animal sacrificed. *Autopsy.*—The fascia edges had blended with the peritoneum. It was thickened but otherwise seemed normal. There was a small omental adhesion.

Histology.—(Microscopic examination.) The sections showed normal, well nourished fascia.

Experiment 46.—Male, yellow and white mongrel; about 1 year old.

Operation.—March 23, 1911. A section of the abdominal wall 3 x 7 cm., including everything except the skin, was excised. Into the peritoneal defect was sutured a flap of fascia lata from one thigh, and into the muscle defect a flap from the other thigh. The skin was closed in the usual manner. Dry dressing. Condition on leaving the table excellent.

The animal developed distemper three days after the operation and on the fifth day the skin wound broke down. There was no hernia as the fascia held firmly.

April 6. Death from distemper. *Autopsy.*—There was a crater like ulcer whose base was made up of fascia on which granulations could be seen both at the edges and scattered over the surface. There was no hernia whatever and the fascia seemed to be strong and intact. On opening the abdominal cavity there was free pus and this was also found in the pleural cavity. The omentum was adherent over a small part of the fascia. The fascia was incorporated with the peritoneum and had healed firmly in position.

Histology.—(Microscopic examination.) The sections showed infiltration with leucocytes, and marked signs of infection. The fascia was apparently in good condition with clearly stained fibers and nuclei. There was definite granulation tissue growing from the ulcer edges out on the fascia.

Comment.—This group shows that free flaps of fascia may be sutured into peritoneal and muscle fascia defects in the abdominal wall, and that it will incorporate itself with the surrounding peritoneum and muscle edges. A small omental adhesion was present on examination of the specimen in each instance, but in no case was there adhesion of the gut or any other abdominal organ to the fascia.

When a hernia was produced by the removal of a portion of the abdominal wall, except the skin, it was readily cured several weeks later by the transplantation of fascia flaps.

These experiments suggest the use of fascia flaps in the cure of large hernia where the muscle is atrophied, and for strengthening any weakened area in the abdominal or chest wall. The facility with which the fascia unites with the peritoneum suggests its further use in pleural and pericardial defects.

Group VII.—Transplantation of Free Fascia onto Stomach, Intestine and Bladder.

Experiment 23.—Female, brown and black mongrel; about 1 year old.

Operation.—January 10, 1911. The bladder was brought up through a mid-line incision and a flap of fascia lata was sewed to it with a continuous suture. The bladder was dropped back and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

July 27. Animal sacrificed. *Autopsy.*—There were omental adhesions to the fascia. The peritoneum on the surface of the bladder was somewhat puckered under and immediately around the fascia edges. The fascia itself was thickened but otherwise seemed normal.

Histology.—(Microscopic examination.) Normal staining fascia found. The peritoneal covering of the bladder could not be differentiated.

Experiment 24.—Female, yellow mongrel; about 6 months old.

Operation.—January 16, 1911. The stomach was exposed and an incision 3.5 cm. long was made in it, down through the mucosa. This was then closed with the Cushing continuous stitch and over the suture line was placed and sutured a flap of fascia lata. The stomach was dropped back and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

January 27. Distemper, animal sacrificed. *Autopsy.*—The fascia was thickened but otherwise seemed normal. It was closely adherent to the stomach wall. There were a few omental adhesions to the fascia but these could be easily separated.

Histology.—(Microscopic examination.) The sections showed the line of suture. Above this was the layer of fascia which was apparently normal and well nourished.

Experiment 61.—Male, black and white fox terrier; about 1 year old.

Operation.—June 5, 1911. A loop of gut was brought up through an abdominal incision and a purse string suture was placed opposite the mesentery. When the suture was drawn tight and tied the portion within the suture projected outward. The tip of the projection was cut off exposing the lumen of the bowel. Over this area a flap of fascia lata was sutured snugly and the gut was dropped back. The wound was closed in the usual manner. Dry dressing. *Per primam* healing.

July 3. Animal sacrificed. *Autopsy.*—The omentum was adherent to the fascia but this was easily separated. The fascia was somewhat thickened but otherwise seemed normal. It was closely adherent and seemed incorporated with the peritoneum of the bowel. There was a definite puckering of the wall of the gut around and under the fascia. There had been no leakage From within a small depression in the mucous membrane corresponding to the pucker made by the purse string could be seen.

Histology.—(Microscopic examination.) The sections showed normal staining, well-nourished fascia. There was marked infiltration of the tissue beneath the fascia with polynuclear leukocytes. There was a great mass of these cells in the area corresponding to the made defect. On the surface of the fascia was the remains of the adherent omentum.

Comment.—In this group free fascia flaps were successfully transplanted onto the stomach, the intestine and the bladder. The fascia seemed to incorporate itself with the peritoneum (Fig. 10).

(a)

(b)

(c)

Fig. 10.—*Experiment 19.* (a) Fascia in peritoneal defect. Operation, December 29, 1910. Specimen removed, February 7, 1911. *Experiment 23.* (b) Fascia on bladder. Operation, January 10, 1911. Specimen removed, June 27, 1911. *Experiment 61.* (c) Fascia over defect in intestine. Operation, January 5, 1911. Specimen removed, July 3, 1911.

In all of these the fascia was thickened. It was incorporated with the peritoneum and there was a puckering of the peritoneum at the margin of the fascia. There was adherent omentum in each case. A small tag can be seen in (a).

Clinically fascia might be used to strengthen suture lines and weakened areas due to ulceration. It might also be of use in closing fistulæ of one sort or another.

Group VIII.—Transplantation of Free Fascia on Liver, Kidney and Spleen.

Experiment 36.—Female, brindle mongrel; about 18 months old.

Operation.—February 21, 1911. Through a lumbar incision the left kidney was exposed and after the capsule was stripped back an abrasion of the surface was made and a flap of fascia lata was sutured over it. The hemorrhage ceased promptly. The kidney was dropped back and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

March 7. Distemper, animal sacrificed. *Autopsy.*—The skin wound which had apparently healed became infected after the development of the distemper. The fascia was adherent to the surrounding tissues. It was not much thickened and seemed normal. It was tightly adherent to the kidney at the edges, but could be stripped up more easily in the center of the flap.

Histology.—(Microscopic examination.) The sections showed normal fascia closely adherent to the parenchyma.

Experiment 52.—Male, black mongrel; about 3 months old.

Operation.—May 8, 1911. Through a high mid-line incision a lobe of the liver was exposed. The end of the lobe was cut off with scissors leaving a bleeding area 3 cm. x 6 mm. Over this surface was placed a flap of fascia lata and the bleeding was markedly checked. The fascia covered the end like a shallow cap, and was held in position by mattress sutures passing through the liver substance and through both sides of the fascia. These sutures were drawn as tight as desired and did not cut through the liver substance. The liver was dropped back and the wound was closed in the usual manner. Condition on leaving the table excellent. *Per primam* healing.

June 6. Death from pneumonia. *Autopsy.*—There was adhesion of the omentum to the fascia. When this was stripped off the fascia was seen covering the denuded area like a cap. It was slightly thickened but otherwise seemed normal.

Histology.—(Microscopic examination.) The sections showed normal staining, well-nourished fascia surrounding an area of liver substance. It was adherent to a considerable extent.

Experiment 60.—Black and white fox terrier; about 1 year old.

Operation.—June 5, 1911. The spleen was brought up through a left rectus incision, the edge was trimmed with scissors, and a flap of fascia was sutured over the denuded area so as to bind it. The fascia was held with mattress sutures which passed through the spleen and both edges of the fascia. There was considerable hemorrhage until the fascia was applied and the sutures tied. The spleen was dropped back and the wound was closed in the usual manner. Dry dressing. Condition on leaving the table excellent. *Per primam* healing.

July 3. Animal sacrificed. *Autopsy.*—The fascia was thickened and securely bound the edge of the spleen. It seemed well nourished and it could be separated from the spleen quite easily.

Histology.—(Microscopic examination.) Sections showed normal staining fascia surrounding spleen tissue.

Comment.—In this group free flaps of fascia were successfully transplanted on the liver, kidney and spleen. It suggests that the fascia flaps might be used to support sutures in these organs, and also to bind raw post-operative surfaces (Fig. 11).

It is to be noted that the fascia when applied to a bleed-

ing surface seemed to have a definite hemostatic effect which is comparable to the hemostatic action of bits of muscle, spoken of by Cushing.

The kidney might be suspended to the ribs or muscles in a sling of free fascia. These results are very promising.

(a)

(b)

FIG. 11.—*Experiment 25.* (a) Fascia on a lobe of the liver. Operation, January 17, 1911. Specimen removed, January 26, 1911. The fascia was thickened but was adherent to the liver surface over most of its extent. *Experiment 36.* (b) Fascia on kidney cortex. Operation, February 21, 1911. Specimen removed, March 7, 1911. The fascia is closely adherent to the kidney substance and blends with the capsule.

In both of these specimens, as in all the others, the fascia was well nourished.

Remarks.—In none of the animals have I noted a muscle hernia after the fascia was removed, but should it occur the hernia could be repaired without difficulty. There is apparently no untoward effect after removal of the fascia lata as far as the use of the limb is concerned.

In every instance the fascia retained its own structure and seemed well nourished. After removal from its bed it was as tough and strong as when first transplanted.

The great strength of the fascia, and, in addition, its thinness and flexibility are to be noted. It can be sutured into a defect under considerable tension, and the sutures will hold securely even when inserted close to the edges or ends of the flap.

The great supply of this material and the ease with which it can be obtained are important points.

There is some difference in the measurements of flaps of fascia before and after removal. For example: A marked out flap of fascia lata measured 4.5 x 2.5 cm. before removal, and after removal it measured 3.3 x 2 cm. Another flap measured before removal 4.5 x 2.2 cm. and after removal 4 x 1.75 cm.

In several experiments fascia was drawn taut and sutured around firm rubber tubes 0.8 to 1 cm. in diameter, and then inserted in the subcutaneous tissue. These specimens were removed after forty-nine and fifty-four days. The structure of the fascia could easily be seen. Microscopic examination showed normal staining fascia with no signs of degeneration.

This is interesting as it shows that fascia will receive sufficient nourishment if only one surface is exposed to living tissue.

The type of so-called distemper prevalent in the laboratory this winter appeared to have some effect on the healing of the wounds and a number of them became infected. This did not seem due to a break in technic, as other animals operated on the same morning (before and after these animals), with identical technic, and not developing the distemper, did not break down.

In several animals whose stitches had been removed after per primam healing the skin wound subsequently broke down after the development of distemper.

In the instances where there was infection the transplanted fascia seemed particularly resistant to it, and retained its structure after the breakdown of the surrounding tissues.

Where there was tension on the fascia there was comparatively little thickening, but wherever the fascia was simply laid on a tissue there was always thickening, and unless it was held flat with sutures it had a tendency to bunch or roll up.

Once or twice the fascia flap was accidentally allowed to partially dry out before it was transplanted, but, in spite of this, it was moistened with salt solution and transplanted. The results were excellent and the fascia was nourished and grew in its new position.

The question naturally arose as to the necessity of transplanting the fascia immediately, and also whether fascia from one animal could be successfully transplanted into another.

Experimentally, both of these questions have been answered satisfactorily.

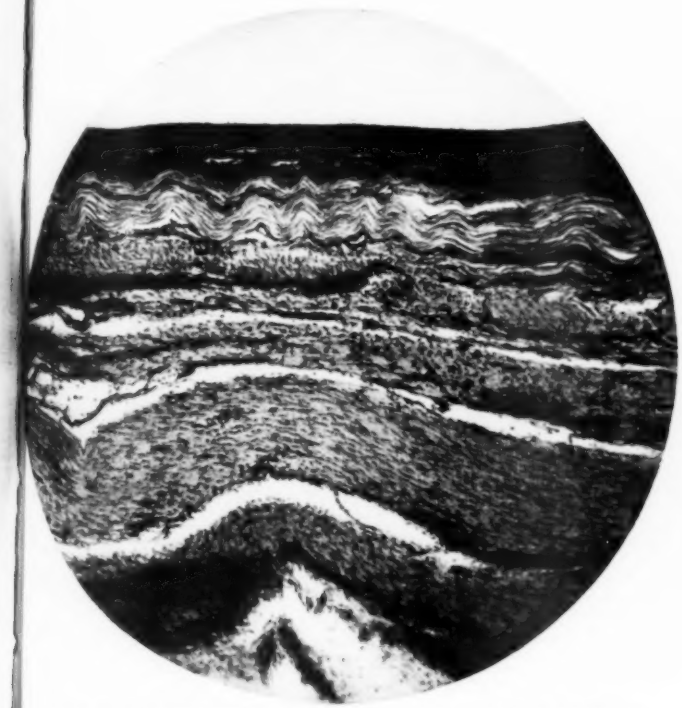


FIG. 5.—(Microphotograph, Zeiss. Obj. AA. Oc. 3.) Two layers of fascia filling defect left by removal of patella. Section cut parallel to fascia bundles. The smooth dark staining layer at the bottom of the plate is the portion toward the joint cavity.

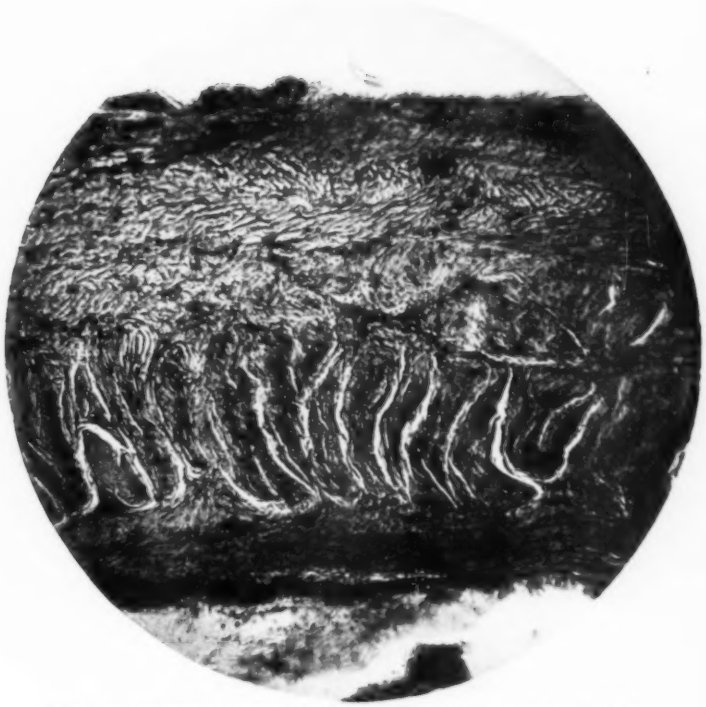


FIG. 12.—(Microphotograph, Zeiss. Obj. AA. Oc. 3.) Fascia preserved in cold storage wrapped in moist salt gauze for 35 days and then transplanted on the surface of a trachea. Operation, March 14, 1911. Specimen removed, April 10, 1911. The section is cut across the fascia bundles. The fascia is normal in appearance and stains well.

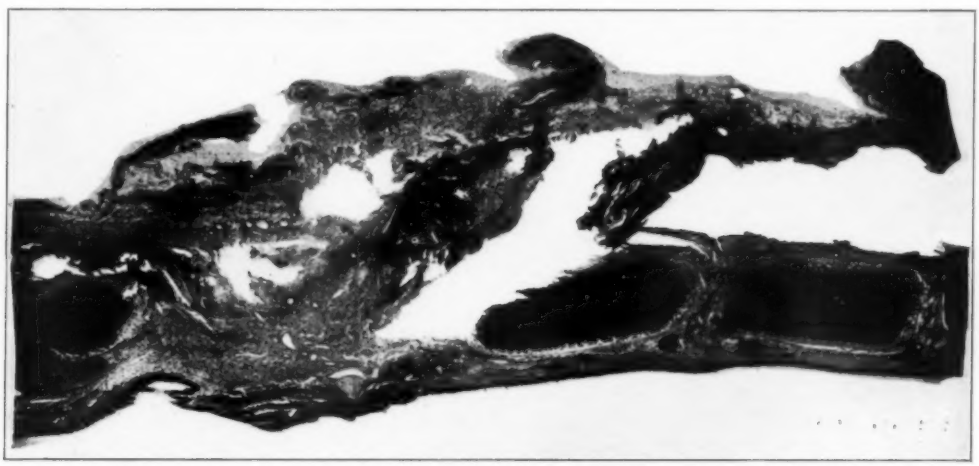


FIG. 9.—(Microphotograph, Zeiss. Obj. AA. Oc. 3.) Longitudinal section of fascia covering a tracheal defect. The defect can be seen between the tracheal rings. On the right of the plate the fascia has become accidentally separated from the surface of the trachea during the preparation of the section. The mucous membrane can be seen covering the fascia.

Fascia was successfully transplanted into the same and other animals after being kept in an ordinary ice chest at 38° C. for as long as seven days; in cold storage at 32° C. wrapped in gauze moistened with salt solution for thirty-five days, and in cold storage at 32° C. in normal salt solution for fifty-six days. (Fig. 12.)

I am sure that the number of days given here does not show the greatest time that fascia may be preserved by the methods spoken of, but I mention the periods as a suggestion that suitable fascia might be preserved until needed for clinical use.

Fascia kept in salt solution appeared edematous when first removed from the solution, but the edema disappeared when the tissue was pressed with dry gauze. The edema was entirely in the superficial connective tissue which had not been removed. The fascia kept in moist salt gauze, on the other hand, was normal in appearance.

When fascia was sutured to the surface of the stomach, intestine or bladder within a few days there was the appearance of puckering or drawing up of the surface under the fascia and at its edges, somewhat similar to the effect of ordinary collodion on the skin. On this area, from within the organ, this puckering was not to be found and the lumen was in no way encroached upon.

The hemostatic action of free fascia flaps is noteworthy.

Conclusions.—The foregoing experiments give an idea of the great possibilities of transplanting free flaps of fascia and many suggestions for the clinical use of this substance may be drawn from them.

I feel convinced that many of the difficult situations arising during operations for the repair of weakened and defective tissues or for the control of bleeding surfaces will be simplified by the use of free fascia flaps and shall report the results of its use in such cases, with a consideration of the literature, in a subsequent paper.

NOTES ON NEW BOOKS.

Progressive Medicine. Edited by Hobart Amory Hare, M. D., etc., assisted by Leighton F. Appleman, M. D., etc. Vol. II. June, 1911. (*Lea & Febiger: Philadelphia and New York, 1911.*)

Coley contributes the chapter on "Hernia," Gerster that on "Surgery of the Abdomen, Exclusive of Hernia," Clark that on "Gynecology," Stengel that on "Diseases of the Blood, Diathetic and Metabolic Diseases; Diseases of the Thyroid Gland, Nutrition, and the Lymphatic System"; and Jackson that on "Ophthalmology." It is interesting in looking over these quarterly volumes to consider how much or how little of all the literature is of permanent value; and whether an annual volume of limited size might not be of greater value; but *Progressive Medicine* is well edited and satisfies a natural demand of the profession.

A Textbook of Nervous Diseases. By William Aldred Turner, M. D. (Edin.), and Thomas Grainger Stewart, M. B. (Edin.) Price, $6. (*Philadelphia: P. Blakiston's Sons & Co., 1910.*)

This book contains 607 pages, including the index. It is well printed, well illustrated, and well bound, opening well, but the unusual purple color of the binding is somewhat startling at first. The work is divided into nineteen parts, instead of chapters, as follows: Anatomy and Physiology, Examination of the Nervous System in a Case of Nervous Disease, The Special Senses, The Cranial Nerves, The Peripheral Nervous System, The Diseases of the Brain, Diseases of the Membranes, Diseases of the Spinal Cord, General Diseases of the Nervous System, Vasomotor and Trophic Diseases, Familial Diseases, Diseases Characterised by Disorders of Muscular Function, Diseases of Obscure Origin Characterised Chiefly by Disorders of Motion, Migraine and Periodic Headache, Hysteria, Neurasthenia, Psychasthenia, Epilepsy, and The Tics. It will be generally agreed that the above arrangement is an excellent one and examination of the work proves it. The authors have so often shown their ability to do excellent work in the past that it goes without saying that they have kept up their reputation in this more ambitious undertaking. We find but little to criticise and that of a trivial nature. Here and there it would perhaps have been better to have enlarged somewhat on certain statements or to have gone more into details but of a necessity brevity would have been sacrificed. One statement we feel should be modified and this appears in two forms, one on page 402, in speaking of the cerebro-spinal fluid, of progressive general paralysis: "The lymphocytes are greatly increased in number—to 150 or 200 or more [per] c. mm. of fluid—and the Wasserman reaction is present in 90 per cent or more of the cases (Mott)." And again on page 553 in discussing the diagnosis of neurasthenia from the neurasthenic type of early paralytic dementia it states as follows: "This occurs chiefly in adult males who have had syphilis. Such cases may, or may not, present physical signs of organic disease, such as loss of the tendon jerks, or reflex pupillary immobility. If these signs are found in association with neurasthenic symptoms, the onset of paralytic dementia may almost with certainty be diagnosed. The failure to obtain these signs of organic disease does not necessarily exclude the onset of paresis; therefore in those cases a lumbar puncture ought to be done and a cytological examination made of the cerebro-spinal fluid. If, on examination of the centrifuged deposit, the lymphocyte count shows 150 to 200 or more lymphocytes, the diagnosis of general paralysis may be made with complete assurance. Although an increase of the lymphocytes is present in most cases of cerebrospinal syphilis, yet the count is rarely so high as in the parasyphilitic diseases." The first statement is not entirely clear as the word *per* is evidently omitted between "more" and "c. mm.," but in regard to both of them we believe that the number is entirely too high, that with such a high count other organic symptoms will undoubtedly be present, and that no competent observer would be willing to make a diagnosis of paresis on a high lymphocyte count alone, no matter how high it might be.

American Practice of Surgery. Editors: Joseph D. Bryant, M. D., LL. D. Albert H. Buck, M. D., vol. VIII. Profusely illustrated. (*New York: William Wood and Co., 1911.*)

With this volume this stupendous system of nearly 9000 pages comes to an end. Both editors and publishers can feel well satisfied with the work, which covers the entire field of surgery as completely, or even more so, than any other system in English. Those who use it will be able to find what they want in it, except that the index is very incomplete, which is a serious defect in such a work. This volume includes chapters on Introthoracic Surgery, Surgery of the Spleen, Surgical Diseases and Wounds

of the Kidneys and Ureters, Surgery of the Pancreas, Surgery of the Liver, Gall-Bladder, and Biliary Passages, Surgical Diseases, Wounds and Malformations of the Urinary Bladder and the Prostate, Surgery of the Ovaries and Fallopian Tubes, Surgery of the Uterus and its Ligaments, Extra-Uterine Pregnancy, and the Caesarian Section and its Substitutes. There are additional sections on The Law in its Relation to the Practice of Surgery, and Administrative Surgical Work, the latter including surgical needs of hospitals, and military, naval and railroad surgery. There is finally an Appendix with a chapter on the Relation of Blood-Pressure to Surgery, and a General Index.

Handbook of Treatment for Diseases of the Eye (Ophthalmic Therapeutics). By DR. CURT ADAM, Berlin. With a preface by PROF. VON MICHAEL, Berlin. Translated from the second German edition (1910) by William George Sym, M. D., etc., and E. M. Lithgow, M. B., etc. Illustrated. Price, $2.50. (*New York: Rebman Company, 1911.*)

This little book is devoted to the *treatment* of the diseases of the eye. While the propriety of separating the treatment from the description of the diseases may be questioned, yet it is sometimes very convenient, and it is possible some may like this book very much.

The treatment advocated for the various eye diseases is usually good, and will be found to give good results. The book states very definitely how to treat the various eye diseases, and if the instructions were even blindly followed the results would in almost every case be good and we suppose this means the book will be of value to some readers whose personal experience in such matters is small and who must necessarily follow some formal and definite plan in treating each disease. To all such readers we can commend this book as being about the best and safest of its class.

The Principles and Practice of Bandaging. By GWILYM G. DAVIS, M. D., etc. Third Edition, Revised. Illustrated. Price, $1. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

This work, which originally appeared in 1891, has been largely rewritten and the illustrations have been redrawn, so that it is practically a new book. As it exists to-day it is a first-rate guide for beginners as the author intends it to be. The drawings and text are both clear, so that a student should have little difficulty in mastering these principles. The author has divided his work into three parts: The Roller Bandages, The Tailed Bandages or Slings, and the Handkerchief Bandages. This arrangement with an abundance of illustrations makes it easy to acquire the practice of bandaging. The compactness and general excellence of this small manual will make it welcome to students.

Fractures and Their Treatment. By J. HOGARTH PRINGLE, M. B. (Ed.), F. R. C. S. (Eng.), Glasgow. Price, $5.50. (*London: Henry Frowde and Hodder & Stoughton, 1910.*) *Oxford Medical Publications.*

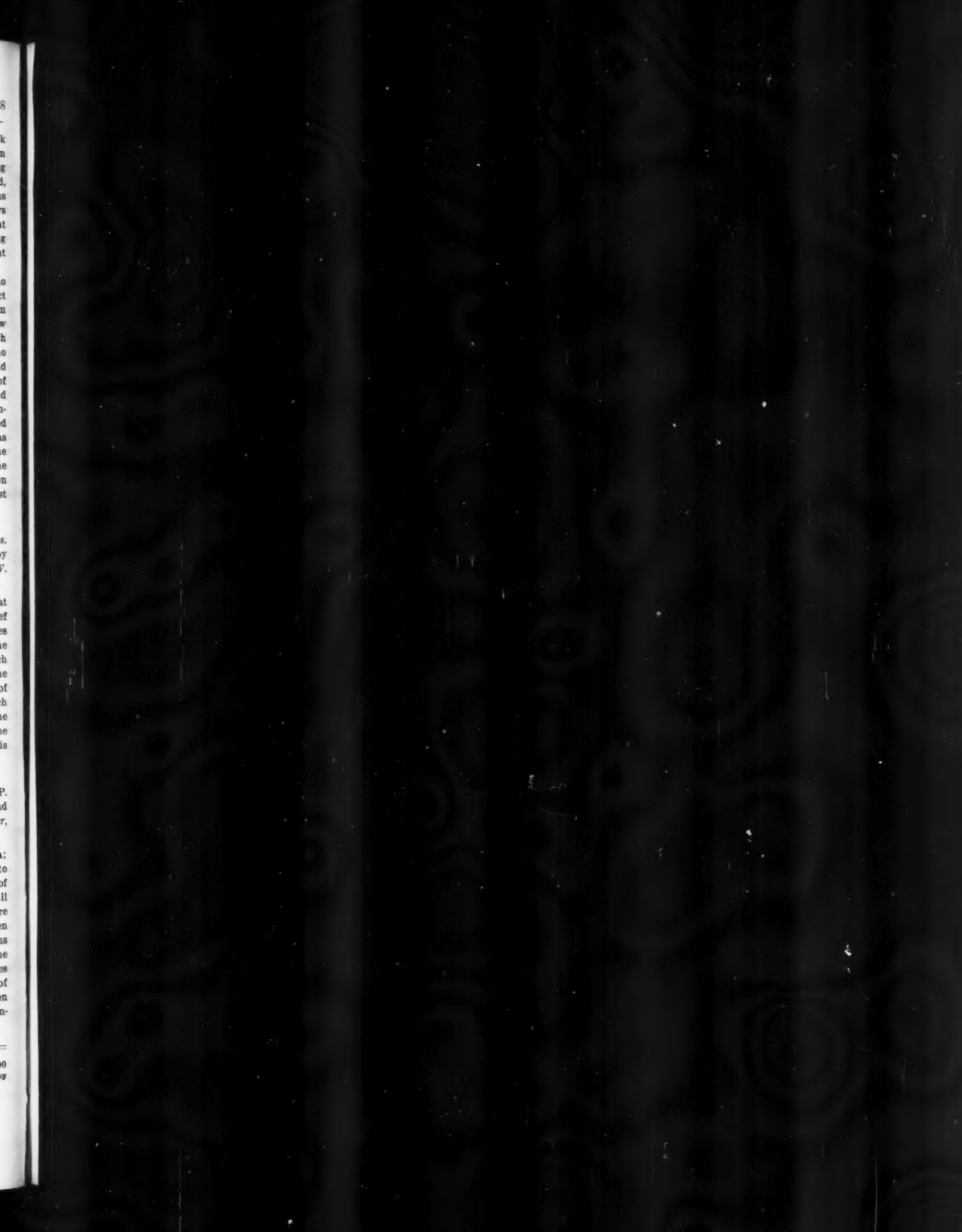
This book deals first with the general facts in relation to fractures. The usual causes, mechanisms, classification, and general diagnostic signs are discussed in the earlier chapters. Following this is a consideration of the process of repair, and of associated lesions of soft parts and joints. Fractures of particular bones are then described, with the methods of treatment, the anatomical sequence of the skeleton being pursued. The final chapter is devoted to the relation of fractures to the Workmen's Compensation Acts of England. At the end of the book are presented several tables, compiled from various German authorities, indicating the amount of depreciation in working efficiency after certain injuries. The book is well illustrated, and contains a good bibliography, the references to special lesions being grouped together. The literary style of the work shows the usual clearness and purity of British authors. The content of the subject-matter is far from being complete, the handling of most of the particular fractures being limited to a statement of general and well-known facts.

One wonders why such a book was written. There seems no reason for this expenditure of time and labor on a subject already so fully and frequently treated, in every form from text-book articles to special volumes, unless there be some new light to shed of importance enough to justify the task. Such illumination, if present, escaped the reviewer. The book has no especial fault except the deadly one of being commonplace and unnecessary. The writer must have sensed the probability of such criticism. In the preface he states that the X-ray and Workmen's Compensation Laws have made of fractures a comparatively new subject, and further says that he was induced to write the book because no special work on the subject has been published in England for a very considerable time. The last reason does not exist in this country, and one feels if the legal aspect of fractures was a prime motive in the construction of the book, that this phase of the subject has been given a most disproportionately small amount of attention. H. B. STONE.

Medical Guide and Monograph Series. Golden Rules of Pediatrics. By JOHN ZAHERSKY, M. D., etc. With an Introduction by C. W. SAUNDERS, M. D. Price, $2.50. (*St. Louis: C. V. Mosby Company, 1911.*)

Although there is nothing on the title page to indicate that this book has appeared before, the author has written a brief "Preface to the Second Edition," which proves that his rules have been welcome to certain members of the profession. The book has been carefully prepared and contains precepts which are serviceable to the student. One might apply, however, the aphorism to "Golden Rules" of this and other branches of science "that all is not gold that glistens." The success of such works is rather a sad reflection on the mental attitude of the doctor who finds them useful. If he knows his science as he should do he will not need them; and unless he knows his science "Golden Rules" are but a snare and delusion.

A Monograph of the Anopheline Mosquitoes of India. By S. P. JAMES, M. D., etc., and W. GLEN LESTON, M. D., etc. Second Edition. Rewritten and enlarged. (*Calcutta: Thacker, Spink & Co., 1911.*)

Although this treatise is intended mainly for workers in India; yet there is so much valuable information in it in regard to mosquitoes, that all students interested in the transmission of contagious diseases, especially yellow fever and malaria, will prize it highly. Its most beautiful and copious illustrations are of immeasurable help in appreciating the differences between the genera. The book is divided into two parts. Part I contains three chapters: 1, A general account of mosquitoes; 2, The collecting, mounting and examination of anopheline mosquitoes and their larvæ; 3, The classification and identification of Indian anophelines. Part II contains the description of thirteen genera. Drs. James and Liston are to be most warmly congratulated on their admirable piece of work.

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